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Index

PTOSIS CONGÉNITAL SIMPLE
DANS 5 GÉNÉRATIONS[1])

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Par ptosis, on entend la chute de la paupière supérieure. Les personnes qui en sont atteintes se trouvent contraintes de pencher la tête en arrière et de baisser les yeux pour compenser cette déficience. S'ils sont touchés unilatéralement, ils ne sont pas obligés de recourir à cette position pour voir. Une atteinte plus légère peut être compensée par une contraction des muscles frontaux, provoquant ainsi une certaine élévation des paupières inertes. Cette correction se produit seulement à partir d'un certain âge, en fonction du développement psychique (*Wilbrand* et *Saenger*, 1900). Une ptose incomplète provoque simplement un aspect particulier du visage conférant au patient un air endormi, sans que sa vision en soit gênée de quelque façon.

Le ptosis héréditaire est en général congénital. Il existe des cas rares où la manifestation peut survenir tardivement (ptosis familial tardif). Sans l'aide de l'histoire familiale, ces cas peuvent être confondus avec le ptosis acquis dû à une affection des systèmes nerveux ou musculaire. Rappelons encore que certaines maladies héréditaires du système nerveux peuvent également s'accompagner d'un ptosis tardif (hérédoataxie, myasthénie, etc.).

Le *ptosis héréditaire congénital* peut être subdivisé en cinq groupes principaux:

1. ptosis simple (isolé);
2. ptosis avec épicanthus;
3. ptosis avec paralysie partielle ou totale du droit supérieur;
4. ptosis combiné avec ophtalmoplégie;
5. ptosis combiné avec d'autres anomalies.

Toutes ces formes de ptosis se transmettent généralement de façon dominante (*Franceschetti*, 1930).

D'après *Wildbrand* et *Saenger*, les facteurs pathogéniques suivants peuvent être à l'origine d'un ptosis:

1. une hypoplasie du muscle releveur de la paupière supérieure;
2. une bifurcation de ce muscle;
3. une adhérence du releveur au droit supérieur;
4. une insertion anormale du releveur;
5. du tissu conjonctif se substituant au tissu musculaire;
6. une absence complète du muscle;
7. une absence de l'innervation périphérique;
8. une aplasie des noyaux oculo-moteurs.

Il est généralement admis, aujourd'hui, que le ptosis héréditaire simple est d'origine myogène, dû à une déficience (hypo- ou aplasie) du muscle releveur (*Berke*, 1945).

L'anatomie comparée et l'embryologie montrent que l'apparition des muscles extrinsèques de l'oeil est en rapport étroit avec la formation du bulbe, chez les vertébrés inférieurs ainsi que chez les supérieurs. Le muscle releveur est le dernier qui apparaît au cours du développement phylogénétique (*Collins*, 1922; *Waardenburg*, 1930; *Walls*, 1942). Il est connu que les acquisitions les plus tardives sont plus facilement susceptibles d'un développement anormal.

Au point de vue ontogénétique, le releveur apparaît relativement tard. La première ébauche des muscles oculo-moteurs se trouve au stade de 7 mm (cinquième semaine de la vie embryonnaire). Un peu avant le stade de 20 mm (septième à la huitième semaine), on peut distinguer les quatre muscles droits et les deux obliques. Le releveur se développe, peu après ce stade, depuis la partie médiane du droit supérieur. Sa position définitive est fixée vers le quatrième mois.

Le ptosis congénital simple est relativement rare. La paralysie palpébrale s'associe en général à d'autres anomalies oculaires et en particulier à l'épicanthus et à l'ophtalmoplégie partielle ou totale. Parfois, on trouve une syngénèse des releveurs avec les droits supérieurs (*Kenel*, 1943), occasionnant un ptosis. Le ptosis peut aussi être accompagné d'autres malformations. Parmi les plus fréquentes, citons la polydactylie (*Giri*, 1943; *Walsh*, 1947), la surdité (*Walsh*, 1947), l'endognathie (*Renard, G., Gornouec* et *J. Renard*, 1948).

Une très ancienne observation de ptose congénitale simple, datant de 1795, nous vient d'un pasteur hollandais, *Martinet*, qui a décrit 9 personnes atteintes dans quatre générations. (Cet arbre généalogique a été repris par *v. Seters* en 1930; cité par *Waardenburg*, 1932). *Horner* (1889) mentionne très brièvement une famille suisse atteinte de ptose simple dans trois générations. Parmi les auteurs qui, depuis, ont trouvé des ptoses congénitales simples, nous mentionnerons: *Addario La Ferla*, 1913 (trois générations), *Briggs*, 1919 (six générations avec 128 personnes dont le 50 % était atteint), *Dimitry*, 1921 (28 cas sur cinq générations), *Krämer*, 1925 (7 cas de ptose dans cinq générations), *Forsberg*, 1932 (cinq générations avec 12 cas), *Biro*, 1934 (trois générations — cependant dans 2 sur 15 de ses cas, on notait une association avec épicanthus).

En général, dans les familles atteintes de ptoses héréditaires, on rencontre des formes bilatérales à côté de cas unilatéraux (*Weissenberg*, 1927; *Killian*, 1923; *Ginzburg*, 1913 et d'autres).

Cependant l'affection peut se manifester parfois de façon exclusivement unilatérale: *Alessi*, 1842, a décrit une ptose unilatérale dans quatre générations. Il est intéressant de relever que la manifestation alternait dans chaque génération (père: à droite; fils: à gauche; petit-fils: à droite; arrière petit-fils: de nouveau à gauche). La même particularité se retrouve dans l'arbre généalogique de *Rodin*, 1936 (quatre générations).

Il faut souligner que le ptosis unilatéral n'est pas accompagné d'épicanthus (*Morganti* et *Musini*; 1948). Par conséquent, dans les familles où l'on trouve des cas unilatéraux, les cas bilatéraux ne sont également jamais compliqués d'épicanthus.

Puisque, mise à part la brève note de *Horner*, il n'existe jusqu'à maintenant, en Suisse, aucun arbre généalogique de ptose héréditaire non compliquée, nous croyons intéressant d'exposer le cas d'une famille dans laquelle on trouve 48 cas, répartis sur cinq générations. Ce travail a aussi pour but de contribuer à la recherche systématique des maladies héréditaires en Suisse.

Observation personnelle.

I. Description de l'arbre généalogique :

La famille Fi.-La. (voir fig. 1) est originaire de N., petite enclave catholique dans le canton de Glaris en majorité protestant.

Les registres communaux, bien tenus, nous ont facilité nos recherches pour établir la généalogie jusqu'au dix-septième siècle.

L'arbre généalogique s'étend sur neuf générations et il nous a été possible de relever les porteurs de cette affection à partir de la cinquième génération.

Etant donné qu'il s'agit d'un caractère héréditaire facilement reconnaissable, les renseignements obtenus des survivants sur les générations précédentes peuvent être acceptés comme sûrs.

L'arbre généalogique commence avec le couple: Johann Kaspar Fi. (II/1; 1717–73) – Maria Anna La. (II/2; 1731–94), dont 3 filles:
Anna Maria Fi. (III/1; 1754/1816);
Anna Margareta Fi. (III/2; 1760/1834);
Anna Katharina Fi. (III/3; 1769/1854)
sont à l'origine des trois branches principales (A, B et C) de l'arbre généalogique:

Branche A. Anna Maria Fi. (III/1; 1754/1816). De son mariage avec Joseph Hilarius Fi. (1758/1795), elle a 3 fils:
Georg Anton Fi. (IV/1; 1787/1866);
Fridolin Joseph Fi. (IV/2; 1788/1858);
Fridolin Jakob Fi. (IV/3; 1790/1858)
qui transmettent le facteur pathogénique et sont à l'origine des trois sous-branches (*a, b, c*) de la branche A:

Sous-branche a). Georg Anton Fi. (IV/1; 1787/1866). Sa fille, *Maria Elizabeth Barbara Fi.* (V/1; 1820/1888) présente pour la première fois dans notre arbre généalogique une *ptose bilatérale.* (Renseignements fournis par son fils Melchior, VI/9; né en 1861, lui-même atteint de ptose bilatérale) (fig. 1, photo 1). Dans la descendance de cette malade, on relève en tout, 18 cas de ptosis:
4 cas dans la sixième génération (VI/2, 3, 5, 9);
7 cas dans la septième génération (VII/4, 6, 8, 10, 12, 15, 17);
6 cas dans la huitième génération (VIII/20, 22, 25, 28, 34, 36);
1 cas dans la neuvième génération (IX/4).
On note encore, un sourd-muet (VIII/16) et 2 cas de *pied varus* (VIII/38 et 40).

Sous-branche b). Fridolin Joseph Fi. (IV/2; 1788/1858). Son fils Joseph Anton Fi. (V/2; 1832/1895) a 7 enfants, dont 3 sont atteints de ptose:
Maria Fi. (VI/11; 1859/1917);
Ferdinand Fi. (VI/13; 1863/1935);
Fridolin Fi. (VI/15; 1867/1948).

Leurs enfants ne sont pas affectés; par contre dans la génération de leurs petits-enfants (génération VIII) on trouve 9 cas de ptosis (VIII/43, 46, 48, 49, 51, 55, 59, 64 et 65), puis 1 cas dans la génération IX (IX/7). (Le cas IX/13 appartient à la branche C – voir plus bas.)

Dans la sous-branche *b*), 2 cas offrent encore quelques particularités:

1. *Joseph Fi.* (VIII/51, né en 1922): *ptose bilatérale* opérée des deux côtés, à l'âge de 8 ans. Il a été reexaminé à la Clinique Ophtalmologique de Genève, en mai 1949, et l'on a noté le status suivant (Pol. No. 3046/49): ptose bilatérale congénitale, exophtalmie de l'oeil droit, prothèse de l'autre côté (enucléation en 1930, à la suite d'un traumatisme) – vision 1,50 de l'oeil droit. Cristallin (o. d.): *cataracte coronaire. Oxycéphalie, palais ogival, implantation irrégulière des dents, acrocyanose des mains et des pieds.*

2. *Wilhelm Fi.* (VIII/59; né en 1943) atteint de ptose unilatérale, décédé dix mois après sa naissance. L'*autopsie* a révélé les constatations suivantes: pneumonie avec augmentation et hypertrophie du coeur, *trou de Botal largement ouvert* (2 cm), *fénestration des valvules aortiques, diverticule de Meckel* d'une longueur de 5 cm et *cryptorchidie bilatérale.* Les parents de ce bébé sont des *cousins au quatrième degré.*

Sous-branche c). Fridolin Jakob Fi. (IV/8; 1790/1864). Dans sa descendance on ne rencontre qu'un atteint (sixième génération): Aloïs Fi. (VI/21; 1865/1933): ptose bilatérale.

Branche B. Anna Margareta Fi. (III/2; 1760/1834). Dans cette branche de notre arbre généalogique, on trouve 3 cas de ptose dans la septième génération: (VII/48, 49, 50) et 2 cas dans la huitième (VII/74 et 79).

Cas VII/48, Joseph Mü., né en 1907, atteint de ptose bilatérale, a un frère, Johann Mü. (VII/41; 1894), qui présente une *surdi-mutité.* En plus, il y a *trois mort-nés* dans cette fratrie. Il est intéressant de noter que les parents (VI/34 et 43) sont des *cousins au troisième degré.*

Branche C. Anna Catharina Fi. (III/6; 1769/1854). Dans cette lignée, on constate dans la sixième génération 3 atteints dans une fratrie (VI/43, 44, 46), 6 restent indemnes et 3 sont morts en bas âge.

A la branche C appartient également le cas IX/13 (Rita V., née en 1948, fig. 1, photo 10). Cependant, bien que son arrière grand-mère (VI/51) fasse partie d'une fratrie dans laquelle se trouvent 3 cas de ptosis (VI/43, 44, 46), il est plus probable que le ptosis de cette malade provient de son père (VIII/61), originaire du canton de Zurich, n'ayant aucune parenté avec la famille Fi-La., mais par hasard, atteint de ptose familiale congénitale. En effet, le père de

Rita V. (VII/37) présente une ptose unilatérale, tandis que son père était atteint de ptosis bilatéral.

Branches collatérales D-E.

A côté de ces trois branches principales (A, B, C) de l'arbre généalogique, on relève une ligne collatérale (D), provenant du mariage de: Johann Fridolin Hau. (I/5; 1706) et de Catherine Bo. (I/6; 1698), tous deux originaires du même village N. Par l'union du petit-fils de ce couple, Joseph Anton Hau. (III/4, né en 1762) avec Anna Margarita Fi. (III/2, née en 1760), cette branche collatérale vient s'adjoindre à la souche principale.

Les deux autres enfants du couple Hau.-Bo. (II/4 et II/5) sont les points de départ de deux autres lignées, indépendantes de la souche principale, dans lesquelles apparaît également du ptosis. En effet, nous trouvons dans ces deux branches, 2 cas de ptose: J. Kaspar Sch. (V/8, né en 1853) et Joseph A. (IX/33, né en 1942). Ce dernier malade a pour père un individu originaire du Tessin (VIII/81) et possédant dans sa famille (E) deux personnes atteintes de ptosis congénital (VII/57 et VIII/83).

Soulignons à ce sujet, cette coïncidence curieuse: deux fois des descendantes non atteintes de la famille Fi.-La. se sont mariées avec des membres de familles totalement différentes d'origine, dont l'un était porteur de l'affection (VIII/61) et l'autre issu d'une famille avec ptosis congénital (VIII/81).

En résumé : on trouve dans l'arbre généalogique (fig. 1) 48 cas de ptosis bilatéral ou unilatéral.

42 cas sont des descendants directs du couple Fi.-La. (II/1–II/2). Sur les 6 autres, 2 appartiennent (VII/37 et VIII/61) à une famille zurichoise liée par le mariage à la famille principale (VIII/60–61). Les 4 autres cas proviennent de deux familles apparentées (branche D et E), dont l'une, D, est autochtone, tandis que la branche E est d'origine tessinoise.

Pour deux cas, l'origine du gène pathologique reste incertaine, puisque dans le cas IX/13 le ptosis peut provenir de la famille zurichoise (VI/18–19), et que dans le cas IX/33 on ne peut pas déterminer si c'est la mère (VIII/80, branche D) ou le père (VIII/81, branche E) qui ont transmis le facteur responsable.

Parmi les 48 cas de ptose congénitale, nous trouvons 24 hommes et 24 femmes; il n'y a donc pas de prédilection de sexe. Sur le total de 48 cas, nous relevons 34 cas de ptose bilatérale et 14 cas unilatéraux.

Etant donné que nous trouvons des malades dans cinq générations de cet arbre généalogique (générations V à IX) et que les deux sexes sont atteints dans les mêmes proportions, on doit conclure à une *hérédité dominante autosomique*. Ceci correspond aux observations faites dans la littérature. Il faut, cependant, relever que cette dominance n'est pas parfaitement régulière, puisque nous trouvons un certain nombre de cas où l'altération génotypique ne se manifeste pas. Ces conducteurs se trouvent presque exclusivement dans la génération VII (VII/5, 21, 28, 32, 34, 38).

Puisque le gène dominant ne se manifeste pas chez tous les porteurs (*dominance irrégulière*), on a le droit de parler d'une *labilité* du gène responsable.

Cette constatation permet d'expliquer en même temps le fait que dans 14 cas sur 48 (29 %), le ptosis n'est qu'unilatéral. En effet, il est connu que les gènes ayant une pénétrance incomplète se manifestent souvent sous une forme unilatérale. Au point de vue clinique, leur expression est également très variable. On trouve ainsi, à côté des formes unilatérales, des formes bilatérales plus ou moins accentuées (*expressivité variable*).

Etant donné que la pénétrance, dans notre arbre généalogique, est incomplète, il nous a semblé indiqué de la calculer selon les méthodes statistiques.

II. *Calcul de la pénétrance :*

Du point de vue statistique, le degré de la pénétrance se calcule de plusieurs façons :

1. la méthode la plus simple est de prendre en considération toutes les fratries atteintes. S'il s'agit d'une dominance régulière, il faudrait trouver dans 100 % des cas, des parents atteints. Dans le cas d'une pénétrance incomplète un certain nombre d'enfants proviendrait de parents indemnes.

En comparant le nombre des fratries où la transmission est directe (pénétrance complète) avec le nombre total des fratries atteintes, on obtient le degré de la pénétrance. D'après le tableau 1 on voit qu'il y a 12 fratries atteintes dont l'un des parents est également affecté, sur un total de 21 fratries atteintes. La pénétrance (P) est donc:

$$P = \frac{12}{21} = 57,1\,\% \pm 10,8\,\%.$$

Tableau 1.

Famille No. voir fig. 1, arbre généalogique	Nombre total des enfants	Enfants atteints	Parents atteints	Parents non atteints	Parents atteints, enfants non atteints
I.	1	1	?	?	
II.	1	1	?	?	
III.	6	4	+		
IV.	6	3	?	?	
V.	11	1	?	?	
VI.	9	3	?	?	
VII.	4	2	+		
VIII.	2	2	+		
IX.	8	3	+		
X.	3	0	+		+
XI.	10	0	+		+
XII.	4	0	+		+
XIII.	3	0	+		+
XIV.	12	0	+		+
XV.	5	1	+		
XVI.	4	2		+	
XVII.	4	1		+	
XVIII.	7	0	+		+
XIX.	6	0	+		+
XX.	8	3		+	
XXI.	3	1	+		
XXII.	1	0	+		+
XXIII.	3	2		+	
XXIV.	7	4		+	
XXV.	4	1		+	
XXVI.	6	2		+	
XXVII.	2	1	+		
XXVIII.	3	2		+	
XXIX.	4	0	+		+
XXX.	8	2	+		
XXXI.	2	1	+		
XXXII.	2	1	+		
XXXIII.	1	1	+		
XXXIV.	2	1	+		
XXXV.	1	0	+		+
XXXVI.	3	1		+	
Total	166	47	22 (5?)	9 (5?)	10

Tableau de la répartition des cas de ptose d'après l'arbre généalogique.

2. Une deuxième méthode consiste à comparer, dans les fratries atteintes, le nombre des atteints par rapport au nombre total des enfants. La méthode dont il faut se servir pour corriger l'excès

Photo 1. Melchior L.
1861; Gen. VI/9

Photo 2. Elisabeth H.
1880; Gen. VII/10

Photo 3. Maria L.
1929; Gen. VIII/25

Photo 4. Joseph L.
1913; VIII/28

Photo 5. Rose-Marie M.
1932; VIII/48

Photo 6. Johanna M.
1933; VIII/49

Photo 7. Joseph F.
1922; VIII/51

Photo 8. Erica F.
1933; VIII/55

Photo 9. Ruth E.
1948; IX/7

Photo 10. Rita V.
1948; IX/13

Photo 11. Joseph A.
1942; IX/33

Fig. 1.

Légende: ■ ● = ptosis bilatéral   ◧ ◑ = ptosis unilatéral gauche   ◧ ◐ = ptosis unilatéral droit   ⊡ ⊙ = surdi-mutité   ⬠ = Jumeaux   ③ = nombre d'enfants   ✳ = cas examiné   ⌐ = ligne indiquant la transmission du ptosis
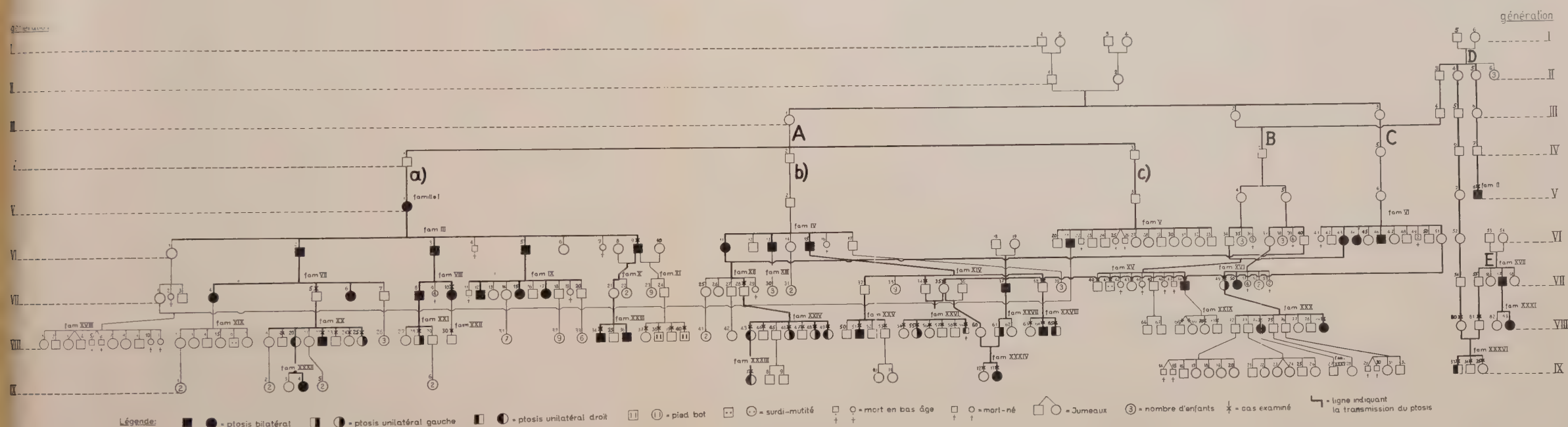
d'atteints est celle de *Weinberg* (,,Geschwistermethode" – voir appendice 2).

Tableau 2. La méthode de *Weinberg* (,,Geschwistermethode").

Famille No.	nombre total (p)	atteints (X)	X (X–1)	X (p–1)
I	1	1	—	—
II	1	1	—	—
III	6	4	12	20
IV	6	3	6	15
V	11	1	—	10
VI	9	3	6	24
VII	4	2	2	6
VIII	2	2	2	2
IX	8	3	6	21
XV	5	1	—	4
XVI	4	2	2	6
XVII	4	1	—	3
XX	8	3	6	21
XXI	3	1	—	2
XXIII	3	2	2	4
XXIV	7	4	12	24
XXV	4	1	—	3
XXVI	6	2	2	10
XXVII	2	1	—	1
XXVIII	3	2	2	4
XXX	8	2	2	14
XXXI	2	1	—	1
XXXII	2	1	—	1
XXXIII	1	1	—	—
XXXIV	2	1	—	1
XXXVI	3	1	—	2

$\Sigma = 26$ $\Sigma(p)=115$ $\Sigma(x)=47$ $\Sigma[x(x-1)]=62$ $\Sigma[x(p-1)]=199$

$$R = \frac{\Sigma X(X-1)}{\Sigma X(p-1)} = \frac{62}{199} = 31\% \pm 3{,}3\%.$$

Chiffre théorique pour dominance = 50 % ± 3,5 %.
Degré de pénétrance : 62 % ± 6,6 %.

La formule est la suivante:

$$R = \sum \frac{X (X-1)}{X (p-1)}$$

X = nombre d'atteints dans chaque famille;
p = nombre total d'enfants dans chaque famille (exclu les enfants morts en bas âge).

On obtient ainsi, pour les 26 fratries de notre arbre généalogique:

$$R = \frac{62}{199} = 31 \% \pm 3,3 \%.$$

Puisque dans la dominance régulière (degré de pénétrance = 100 %) 50 % des enfants doivent être atteints, il ressort que dans notre cas, la pénétrance est de 62 ± 6,6 %. Ce chiffre correspond bien à celui obtenu par la première méthode (= 57,1 % ± 10,8 %) (voir plus haut).

Tableau 3. La méthode directe.

Enfants issus de père ou mère atteints.

Famille No.	nombre (p)	atteints (X)	non-atteints
III	6	4	2
VII	4	2	2
VIII	2	2	—
IX	8	3	5
X	3	—	3
XI	10	—	10
XII	4	—	4
XIII	3	—	3
XIV	12	—	12
XV	5	1	4
XVIII	7	—	7
XIX	6	—	6
XXI	3	1	2
XXII	1	—	1
XXVII	2	1	1
XXIX	4	—	4
XXX	8	2	6
XXXI	2	1	1
XXXII	2	1	1
XXXIII	1	1	—
XXXIV	2	1	1
XXXV	1	—	1
Total 22 familles	96	20	76

$$R = \frac{X}{p} = \frac{20}{96} = 21 \% \pm 4,2 \%.$$

$$\text{Chiffre théorique d'atteints} = \frac{48}{96} = 50 \% \pm 5,0 \%.$$

Pénétrance : 42 % ± 8,3 %.

3. Méthode directe.

Lorsqu'il s'agit d'une dominance régulière, on peut généralement se passer de la méthode de Weinberg en tenant compte du nombre total des enfants provenant de parents atteints, y compris les fratries indemnes, mais issues de père ou mère atteints. Ensuite on peut, sans autre, obtenir la relation entre les atteints et le nombre total des enfants

$$R = \sum \frac{X}{p}$$

Dans notre arbre généalogique, nous pouvons appliquer cette méthode pour les familles dont l'un des parents est atteint. Nous obtenons alors pour 22 familles (dont 12 avec enfants atteints, 10 sans enfants atteints):

$$R = \frac{20}{96} = 21\% \pm 4,2\%.$$

Ceci correspond à une pénétrance de 42 %.

Ce chiffre est nettement inférieur à ceux obtenus par les méthodes 1 et 2. Ce qui est d'autant plus surprenant que la méthode de Weinberg appliquée aux mêmes 22 fratries issues d'un parent atteint, donne un résultat correspondant à celui des autres méthodes.

$$R = \sum \frac{X(X-1)}{X(p-1)} = \frac{24}{73} = 33\% \pm 5,5\%.$$

Ceci correspond à une pénétrance de 66 %.

La différence entre les deux chiffres obtenus pour la pénétrance selon la méthode directe (42 %) et la méthode de Weinberg (66 %) doit provenir du fait que le nombre des fratries indemnes est relativement trop élevé. En effet on est frappé par la constatation que, par exemple, les deux familles (XI et XIV), composées respectivement de 10 et 12 enfants, dont les parents sont atteints, ne présentent aucun membre affecté. Ceci est d'autant plus étonnant que la probabilité qu'aucun membre ne soit affecté à condition que la pénétrance soit de 60 %, est seulement de 2,8 % pour une fratrie de 10 enfants et de 1,4 % pour une famille de 12 enfants.

Du point de vue statistique cette discordance peut s'expliquer uniquement par le jeu du hasard. On peut aussi introduire l'hypothèse d'un facteur inhibiteur qui dans certaines familles empêcherait la manifestation du gène principal plus ou moins labile. Ce facteur pourrait éventuellement provenir du conjoint non atteint.

III. *Association de la ptose avec d'autres affections :*

Un cas présente un intérêt particulier: Willy F., 1943 (VIII/59), mort à dix mois d'une pneumonie. Son autopsie a révélé une ptose, un trou de Botal ouvert, une fénestration des valvules aorti-

ques, un diverticulum de Meckel de longueur anormale. Il est important de relever dans ce cas une consanguinité des parents, le père (VII/34) et la mère (VII/35) étant des cousins au quatrième degré [arrière-arrière grand-mère du père (III/1) et arrière-arrière grand-mère de la mère (III/3) sont des soeurs].

En présence des multiples anomalies de cet enfant et de la consanguinité de ses parents, il faut se demander s'il n'existe pas dans ce cas, une homozygotie du gène dominant.

Par contre, il faut souligner que dans un autre cas de mariage consanguin (VII/1 et VI/21) on ne constate aucune anomalie chez les enfants vivants (mais 2 bébés sont mort-nés: VIII/10, 11 et une paire de jumeaux décédés en bas âge: VIII/5, 6).

Chez un seul malade (Joseph F., 1922, VIII/51, photo 7, fig. 1), la ptose était associée à une autre affection de l'oeil, à savoir une *cataracte coronaire*, mais sans diminution de la vision (vision = 1,5). Ce patient présentait en outre une *oxycéphalie* légère, un palais ogival et une *acrocyanose* des mains et des pieds.

3 malades présentaient une amblyopie:

a) VIII/48 (Rose-Marie M., 1932, fig. 1, photo 5), ptose unilatérale gauche. Il existe une amblyopie des deux côtés (vision o. d. = 0,3; o. g. = 0,1);

b) VIII/49 (Johanna M., 1933, fig. 1, photo 6), ptose unilatérale droite, amblyopie unilatérale droite (vision o. d. = 0,1; o. g. = 1,5);

c) VIII/55 (Erica F., 1933, fig. 1, photo 8), ptose unilatérale gauche, amblyopie unilatérale gauche (vision: o. d. 1,25; o. g. = 0,2).

Tandis que dans le cas a), l'amblyopie se présente des deux côtés, mais plus forte du côté du ptosis, dans les cas b) et c) elle se présente uniquement du côté de l'affection.

Aucun des membres examinés de la famille n'offrait de trouble oculo-moteur. En particulier, on ne trouve ni insuffisance du droit supérieur, ni épicanthus. De plus, les examens de la pupille et des réflexes tendineux des membres supérieurs et inférieurs ne révélaient pas d'anomalie.

En conclusion, nous constatons que ce type de ptosis reste constant pour toutes les branches de cette famille, mis à part les différents degrés de pénétrance et d'expressivité.

Il est surtout important de relever que parmi tous les cas examinés, il n'existe aucune combinaison d'un ptosis soit avec une insuffisance du droit supérieur ou un autre muscle oculo-moteur, ou soit avec un épicanthus.

La distinction entre la ptose héréditaire non compliquée et les autres formes de ptose congénitale est donc justifiée.

IV. *Autres affections dans la famille :*

Parmi les anomalies non associées avec une ptose, il faut d'abord mentionner la *surdi-mutité* dans le cas VII/41 (Johann M., 1894). On rencontre dans cette fratrie encore 3 mort-nés (VII/42, 46, 47). La mère de ces enfants (VI/43, Anna Katherine M., 1865) est atteinte de ptose et cousine au troisième degré de son mari, son arrière-grand-mère maternelle (III/3) et son arrière-grand-mère paternelle (III/2) étant des soeurs.

Un deuxième cas de *surdi-mutité*, sans consanguinité démontrée des parents, est VIII/16 (Joseph H., 1922).

La surdi-mutité, dans ces cas est probablement la manifestation d'un facteur récessif indépendant se réalisant pour l'un des cas à cause de la consanguinité des parents.

Deux frères (Anton et Ernest L., 1935, 1940, VIII/38 et 40) présentaient un *pied bot bilatéral*. On ne relève aucune consanguinité chez les parents. Cette affection est probablement aussi due à un facteur indépendant de la ptose.

V. *Récapitulation de tous les cas présentant du ptosis ou d'autres anomalies :*

Génération IX.

IX/4: Maria P., née 1948: ptosis bilatéral faible.

IX/7: Ruth F., née 1948: ptosis unilatéral o. d. Conjonctivite à l'o. g. qui provoque un „pseudo-ptosis" à cet oeil. (Fig. 1, photo 9).

IX/13: Rita V., née 1948: ptose bilatérale (fig. 1, photo 10).

IX/33: Joseph A., né 1942: ptose unilatérale o. d. (fig. 1, photo 11).

Génération VIII.

VIII/16: Joseph H., né 1922: surdi-mutité congénitale.

VIII/20: Judith L., née 1919: ptose unilatérale o. d.

VIII/22: Léo L., né 1923: ptose bilatérale assez prononcée. Contraction des muscles frontaux chez ce malade dès qu'il veut fixer un objet.

VIII/25: Maria L., née 1929: ptose unilatérale o. g. (fig. 1, photo 3).

VIII/28: Joseph L., né 1913: ptose unilatérale o. g. opérée en 1933. Vision o. d. 1,0; o. g.: voit ses doigts à 3 m, par suite d'un traumatisme.

VIII/34: Joseph R., né 1917: ptose bilatérale opérée en 1927.

VIII/36: Aloïs R., né 1928: ptose bilatérale faible.

VIII/38: Anton L., né 1935: pied bot congénital.

VIII/40: Ernest L., né 1940: pied bot congénital.

VIII/43: Ruth F., né 1921: opérée en 1938 d'une ptose très prononcée de l'o. d.

VIII/46: Margareth M., née 1927: ptose unilatérale o. g. opérée en 1943.

VIII/48: Rose-Marie M., née 1932: ptose unilatérale o. g. Vision o. d.: 0,3; o. g.: 0,1 (sans correction) (fig. 1, photo 5).

VIII/49: Johanna M., née 1933: ptose unilatérale o. d. Vision o. d.: 0,1; o. g.: 1,5 (sans correction) (fig. 1, photo 6).

VIII/51: Joseph F., né 1922: ptose bilatérale très prononcée. A part la contraction des muscles frontaux, on note également un rejet de la tête en arrière. Opération en 1922 ddc. Palais ogival, acrocyanose, position irrégulière des dents; oxycéphalie. Examen en 1949 (Clinique Ophtalmologique de Genève, Pol. No. 3046/49): ptosis congénital ddc. Prothèse o. g. Cataracte coronaire o. d. Vision o. d.: 1,50 (fig. 1, photo 7).

VIII/55: Erica F., née 1933: ptose unilatérale o. g. Vision o. d. 1,25; o. g.: 0,2. Amblyopie incorrigible.

VIII/59: Wilhelm F., né 1943: mort en 1944, à dix mois, de pneumonie. Autopsie: hypertrophie du coeur. Trou de Botal ouvert (2 cm), fénestration des valvules de l'aorte, oedème pulmonaire des lobes inférieurs, diverticule de l'ilium de 5 cm, cryptorchidie bilatérale. Ptose unilatérale o. g.

VIII/61: Adolph V., né 1919: ptose unilatérale o. g.

VIII/64: Rudolph F., né 1938: ptose bilatérale plus prononcée à gauche et opérée en 1949. La tendance de rejeter la tête en arrière et de baisser les yeux a persisté après l'intervention.

VIII/74: Elise S., née 1912: ptose bilatérale compensée par la contraction des muscles frontaux et rejet de la tête en arrière.

VIII/79: Pia F., née 1928: ptose bilatérale faible, conférant à la malade un air endormi.

VIII/83: A., ptose bilatérale.

Génération VII.

VII/4: Maria-Magdalena H., née 1882: ptose bilatérale.

VII/6: Lisette L., née 1885: ptose bilatérale.

VII/8: Melchior L., né 1878, mort en 1943: ptose bilatérale.

VII/10: Elizabeth H., née 1880: Ptose bilatérale très prononcée. La fente palpébrale est raccourcie d'une façon extrême. Pour voir, la malade est obligée de rejeter la tête tout en arrière, de baisser les yeux et de contracter les muscles frontaux (fig. 1, photo 2).

VII/12: Melchior L., né 1876, mort en 1945: ptose bilatérale.

VII/15: Catherine L., née 1881, morte en 1943: ptose bilatérale.

VII/17: Louise L., née 1884, morte en 1934: ptose bilatérale.

VII/37: Gottfried V., né 1881, mort en 1946: ptose bilatérale.

VII/41: Johann M., né 1894: surdi-mutité congénitale.

VII/48: Joseph M., né 1907: ptose bilatérale très prononcée. Les pupilles sont à demi-couvertes par les paupières. Une élévation volontaire des paupières supérieures est impossible. Le malade ne réussit à voir qu'en rejetant la tête en arrière et en fronçant les sourcils.

VII/49: Martha G. F., née 1882: ptose unilatérale o. g. Opérée d'une cataracte bilatérale à l'âge de 60 ans.

VII/50: Elizabeth G., née 1883: ptose bilatérale.

VII/57: A., : ptose bilatérale.

Génération VI.

VI/2: Fridolin-Kasimir L., né 1845, mort 1917: ptose bilatérale.

VI/3: Joseph Anton L., 1847–1881: ptose bilatérale.

VI/5: Caspar Fridolin L., 1850–1935: ptose bilatérale.

VI/9: Melchior L., 1861: ptose bilatérale très prononcée (fig. 1, photo 1).

VI/11: Maria M., 1859–1917: ptose bilatérale.

VI/13: Ferdinand F., 1863–1935: ptose bilatérale.

VI/15: Fridolin F., 1867–1948: ptose bilatérale, plus prononcée à droite qu'à gauche.

VI/21: Aloïs F., 1865–1933: ptose bilatérale.

VI/43: Maria Catherine M., née 1865: ptose bilatérale très prononcée.

VI/44: Anna-Agnès F., née 1869: ptose bilatérale.

VI/46: Hermann F., né 1869: ptose bilatérale.

Génération V.

V/1: Elizabeth Barbara F., 1820–1888: ptose bilatérale.

V/8: Johann-Caspar S., 1853–1924: ptose bilatérale opérée en 1916. Strabisme convergent.

Résumé.

Description d'une famille glaronnaise atteinte de ptose héréditaire congénitale simple, se transmettant selon le mode dominant à travers 5 générations.

Le nombre total des malades est de 48, répartis en 24 hommes et 24 femmes. Dans 32 cas la ptose s'est manifestée sous forme bilatérale et 14 fois unilatéralement.

La variabilité des manifestations cliniques du ptosis, les formes unilatérales, ainsi que le fait que l'affection peut être transmise par des individus non atteints, parlent en faveur d'un gène d'expressivité et de pénétrance variables.

Le calcul du degré de la pénétrance donne un résultat d'à peu près 60 %.

Parmi les affections associées à la ptose, on trouve dans 1 cas une cataracte coronaire, combinée avec une oxycéphalie, un palais ogival et une acrocyanose. Un enfant atteint de ptose et mort à l'âge de dix mois présentait lors de l'examen pathologique un trou de Botal ouvert avec fénestration des valvules aortiques et une cryptorchidie. Dans 2 autres cas on trouve une amblyopie du côté de la ptose, dans un troisième cas une amblyopie bilatérale.

Comme affections indépendantes de la ptose, on relève dans l'arbre généalogique 2 cas de surdi-mutité, dont l'un provient d'un mariage consanguin et 2 cas de pied bot.

Dans tous les cas examinés, la ptose n'était jamais combinée avec une insuffisance du droit supérieur ou d'un autre muscle oculomoteur, ni associée à un épicanthus.

Il semble donc justifié de séparer, du point de vue génétique, le ptosis héréditaire simple des autres formes de ptosis héréditaire compliqué.

Summary.

A family of the Canton of Glarus with hereditary congenital uncomplicated ptosis and dominant inheritance through 5 generations is described.

The total number of the patients is 48, 24 being of male and 24 of female sex. In 32 cases the ptosis was bilateral and in 14 cases unilateral.

The variability of the clinical manifestations of the ptosis, the unilateral forms and the fact, that the condition proved to be transmitted by non affected individuals, speak in favour of a gene with variable expressivity and penetrance.

The determination of the degree of penetrance gives a value of about 60 per cent.

Among the affections associated with ptosis, there was one case of coronary cataract, combined with oxycephaly, ogival palate, and acrocyanosis. A child affected by ptosis who died at the age of 10 months, presented at the pathological examination an open foramen ovale with fenestration of the aortic valves, and cryptorchism. In two other cases there existed an amblyopia on the side of the ptosis, in a third case a bilateral amblyopia.

As independent affections of the ptosis, there were two cases of deaf-mutism, one arising of a consanguineous marriage, and two cases of club-foot.

In all examined cases the ptosis was never found combined with weakness of the superior rectus or any other oculo-motor muscle, neither with epicanthus.

From a genetic point of view, it seems therefore justified to separate the hereditary uncomplicated ptosis from the other complicated forms.

Zusammenfassung.

Beschreibung einer Familie aus dem Kanton Glarus mit hereditärer, kongenitaler Ptosis simplex, die sich dominant über 5 Generationen vererbt.

Die Gesamtzahl der Kranken beträgt 48, von denen 24 auf das männliche und 24 auf das weibliche Geschlecht entfallen. In 32 Fällen war die Ptosis beidseitig und 14 Male einseitig.

Die Variabilität der klinischen Erscheinungen der Ptosis, die einseitigen Formen, sowie die Tatsache, daß sich die Krankheit auch durch nicht befallene Individuen übertragen kann, sprechen im Sinne eines Gens von variabler Expressivität und Penetranz.

Die Berechnung des Grades der Penetranz ergab einen Wert von ungefähr 60 %.

Von den mit Ptosis assoziierten Affektionen fand sich in einem Falle eine Cataracta coronaria, die mit Oxycephalie, hohem Gaumen und Akrozyanose kombiniert war. Ein von Ptosis befallenes Kind, das im Alter von 10 Monaten gestorben war, wies bei der pathologischen Untersuchung ein offenes Foramen ovale mit Fensterung der Aortenklappen, sowie einen Kryptorchismus auf. In 2 anderen Fällen fand sich eine Amblyopie auf Seiten der Ptosis, in einem 3. Falle eine beidseitige Amblyopie.

Als von der Ptosis unabhängige Affektionen fanden sich im Stammbaum 2 Fälle von Taubstummheit, davon einer aus konsanguiner Ehe hervorgehend, und 2 Fälle von Klumpfuß.

In allen untersuchten Fällen war die Ptosis niemals mit Insuffizienz des Rectus superior oder einer anderen okulo-motorischen Störung, noch mit Epikanthus kombiniert.

Es rechtfertigt sich somit vom genetischen Standpunkte aus, die Ptosis hereditaria simplex von den anderen komplizierten Formen von hereditärer Ptosis abzutrennen.

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STANDARD ERROR AND MEDICINE

by GUNNAR DAHLBERG

In practical life we are often forced to act on the basis of our sense of probability. Physicians, especially, in time get the habit of making such judgements; they can seldom put off their treatment of the patients until the diagnosis is absolutely safe, but have to draw their conclusions from more or less uncertain information. The so called "doctor's eye" in so far as it exists is probably nothing but a special faculty of correctly judging probabilities. Owing to his experience the older physician often is more successful at this than his younger colleague, and at least partly this compensates him for his less up to date professional training.

Not only in the physician's practice but also in medical research do probabilities play an important part. It is often necessary to draw conclusions from material having a very limited scope and therefore only allowing statements which are probable to a certain degree. At other times, however, the differences are so manifest that statistical methods are rendered unnecessary. The habit of doctors of taking probabilities into account often makes them careful enough to avoid false conclusions. But sometimes the situation is too complicated to be cleared up by common sense alone. I shall give examples of this chosen from an other field.

Suppose that a person has twenty-five friends who usually invite him to birthday parties. How great is the probability that he will be invited to two parties on the same day? The question looks simple but I am fairly sure that most people will answer it wrongly.[1]

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[1] This problem is taken from a book by *George Gamow:* One, two, three, ∞ . The reader may wonder why I use the problem here. I would therefore remind him of the story about Demosthenes. When the people in Athens once did not care to listen to him he said he wished to tell them a little story. "Once upon a time there was a man who wished to go to Megara and therefore hired a donkey and its owner. In the middle of the day when the sun was blazing hot they tried to take a rest in the shadow of the donkey. But the shadow was not large enough for both of them. The owner said that the man had hired only the donkey but not

By adopting statistical methods it is possible to get around the uncertainty inherent in endeavouring to decide without fixed criteria whether or not a material is large enough to permit conclusions to be drawn from it. Statistical methods cannot, however, prevent the material from being chosen in an unintentionally misleading manner. Control investigations may therefore be welcome even if statistical methods have been used. No general rules can be laid down, however, for this side of the matter.

Nevertheless, it is of very great importance to find out whether the material is sufficiently large, in so far as this can be done by the calculation of standard errors etc. As we know, a deviation is considered statistically significant if it is greater than three times the standard error. Even if this rule is followed, however, some, if small, risk is run that the difference is due to random variation. For in one out of 370 cases or in 0.27 per cent a difference may happen to be greater than three times the standard error (provided the distribution is what we call normal). In a hundred or so theses for the doctorate I three times have had reason to suspect that a significant difference actually was due to random variation. If conclusions had been drawn on the basis of differences that only were 2 or $2\frac{1}{2}$ times their standard errors, quite a number of them would certainly have been fallacious. In medicine it is especially important not to draw hasty conclusions if this can be avoided. Since the problems are bound up with the wellbeing of human subjects especial care must be exercised. Moreover, from the statistical point of view it is important that the methods are not discredited by unwarranted conclusions. It is unnecessary to demonstrate that anybody can tell a lie, but a certain amount of erudition is required to create statistics.

In statistics, however, the rule of three times the standard error is internationally accepted. In order to illustrate this, the appended table tells which rules are given by various authors of textbooks.

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its shadow. The man disagreed. He said he had hired the donkey and everything belonging to it, consequently also its shadow." At this point Demosthenes turned round to go away. But the people protested. They were curious about the end of the story. Demosthenes then said: "It is very peculiar that you care to listen when I speak about a donkey but not when I speak about more important things." Then they let him speak and forgot about the donkey. So nobody knows what happened to its shadow.

The authors included in table 1 are those whose works are available in the library of the State Institute for Human Genetics and Race Biology in Sweden and therefore are not selected with any special bias.

Table 1.

Rule for statistical significance according to different text-books.

Author	Year of publication	Rule
Charlier, C. V. L.	1920	3 times the standard error
Mackeprang, E.	1923	4 times the standard error
Westergaard and *Nybolle*	1927	3 times the standard error
Essen-Möller, Erik	1941	3 times the standard error
Liljeström, Alfred	1938	3 times the standard error but he expresses himself vaguely.
Wigforss, Frits	1938	2.6 times the standard error. He mentions also the rule of 3 times the standard error.
Arley, Niels	1940	2 times the standard error
Bonnier and *Tedin*	1940	4 times the standard error implies that the difference is very safe, but they also indicate the degree of safety when the difference is 2 or 3 times the standard error.
v. Hofsten, Erland	1942	3 times the standard error
Kemp, Tage	1942	3 times the standard error but he expresses himself somewhat vaguely.
Jahn, Gunnar	1943	3 times the standard error
Quensel, Carl-Erik	1944	2.5–3 times the standard error
Czuber, Emanuel	1925	3 times the standard error
Weinberg, Wilhelm	1921	4 times the standard error
Winkler, Wilhelm	1931	3 times the standard error
Behrens, Walter-Ulrik	1933	No rule
Weber, Erna	1935	3 times the standard error
Ringleb, F.	1937	3 times the standard error
Czuber-Burkhardt	1938	3 times the standard error
Mittman, Otfrid	1940	No rule
Bowley, Arthur	1920	3 times the standard error
West, Carl J.	1920	3 times the standard error
Whipple, George Chandler	1923	No rule
Secrist, Horace	1929	Expresses himself vaguely.
Davenport, C. D. and *Merle, P.Ekas*	1936	2 times the standard error
Hill, A. Bradford	1937	2.5 or 3 times the standard error
Yule, Udny G. and *Kendall,M.G.*	1937	3 times the standard error

Author	Year of publication	Rule
Arkin, H. and *R. Colton*	1938	3 times the standard error
Baten, William Dorwell	1938	2.6 times the standard error
Elderton, Palm W.	1938	2 times the standard error gives a comparatively great safety.
Lindquist, E. S.	1938	3 times the standard error
Snedecor, George W.	1938	2.5 times the standard error but expresses himself vaguely.
Hays, Samuel	1939	3 times the standard error
Mc Cormick, Thomas	1941	2.5 times the standard error
Mather, K.	1943	2 times the standard error
Garret, Henry E.	1947	2 times the standard error
Hoel, Paul G.	1947	2 times the standard error
Levy, H. V., and *Preidel, E. E.*	1947	No rule
Peatman, John Gray	1947	3 times the standard error
Weatherburn, C. E.	1947	2 times the standard error
Hosemann, H.	1949	3 times the standard error

Before we comment on this table, it should be noted that, of course, there exists no sharp demarcation between what is called statistically significant and not significant. The probability for a difference between two means which refer to different materials taken from the same population decreases continuously according to a normal curve. What odds one is willing to take when neglecting the possibility that the difference may be due to random variation and so not "real" has actually nothing to do with statistics. Largely the answer is a matter of temperament. One person is less inclined to run risks than another, just as one person is more inclined to insure himself than another. The important thing is, however, to have a hard and fast rule which is adhered to consistently. If such a rule is lacking, it can be tempting to disregard the risk to a greater degree when a result is desired that when it is not. A hard and fast rule is furthermore required for all the readers who have no statistical training and are unused to appraising figures. Therefore it is hardly suitable merely to give the probability that the difference is caused by random variation and leave the conclusion to the reader.

We now shall give the rules used in Sweden in some detail. If a difference exceeds 3 times the standard error, the difference between the materials is considered "statistically" significant. If the difference lies between 2½ and 3 times the standard error, the difference is said to be "probable". If the difference lies between one

time the standard error and $2\frac{1}{2}$ times that quantity, the agreement between the materials is thought "satisfactory". Finally, if the difference is less than the standard error, the agreement is said to be "good". It should be noted with respect to differences which are said to be probable that no definite conclusions ought to be drawn from them. On the other hand, it is likely that a larger material would yield a definite difference. Under such circumstances the result is conducive to continued investigation. However, under no circumstances must a formula be attempted which permits passing from a probable difference to a definite statement. The probability for a deviation which exceeds 2 σ is 4.55 per cent. If it exceeds $2\frac{1}{2}$ σ the probability is 1.24 per cent, and for 3 σ the probability, as we have mentioned above, is 0.27 per cent.

From the table it appears that practically all continental textbook authors have accepted the rule of three times the standard error of the mean. Among English and American authors some have remained content with 2 or $2\frac{1}{2}$ times the standard error, while others have gone as far as 3 times the standard error. As a rule the former have been pupils of *R. A. Fisher*. We shall therefore briefly discuss his views.

Previously *Fisher* worked at Rothamsted Experiment Station where botanical genetics were studied. His problem then was to decide whether or not the actual results agreed with the expected figures. In order to be careful, *Fisher* at the time introduced the rule that a result with a discrepancy of more than 2 times the standard error should be considered dubious. Of course this rule is quite reasonable, but it must not be reversed to mean that a difference of more than 2 times the standard error is statistically significant. Yet this is precisely what *Fisher* and his followers did.

In his book "Design of Experiment" *Fisher* takes a somewhat curious position. He maintains that, generally speaking, the statistical problem is to prove agreement between the figures obtained and those to be expected according to a given hypothesis. However, statistical methods only make it possible to prove the absence of agreement, and in general this is the problem in medicine. One desires to demonstrate that diseased persons differ from healthy ones, that patients subjected to some special treatment differ from those not given this treatment, etc. All the time the problem is to show that there is a difference which is not caused by random variation, *not*, as *Fisher* maintains, to show that there is agreement.

(The hypothesis of the absence of difference he calls the O-hypothesis.) Starting from *Fisher*'s position, to demonstrate agreement it would be merely necessary to choose a small enough material. The standard error then becomes so large that the difference becomes less than twice the standard error, and this, according to *Fisher*, would show agreement. When I pointed this out to *Fisher*, he said that one must use common sense and refrain from drawing conclusions from series which are too small. Yet the result of having to determine what constitutes an "adequately large" material in this respect is that one lands right in the middle of the uncertainty and the sub-jectivity one wants to avoid by using statistical methods. Obviously *Fisher*'s contention is wrong. If no difference is obtained, it is theoretically impossible to exclude the possibility of a difference arising in a larger material. All that can be said is that in such a larger material a possible difference must be less than 3 times the standard error in the smaller material and that such a difference can be unimportant. The rule of 2 times the standard error of course implies far greater risks than are involved in keeping to the rule of three times the standard error. Moreover, *Fisher* sometimes seems to have abandoned this rule. He says that one should give the likelihood that the difference is caused by random variation and then leave the reader to decide whether or not he thinks the risk can be neglected. (To obtain the likelihood one may use a so called t-test developed by Student in 1908, which simply gives the pro-bability for a deviation of a given magnitude.) However, as pointed out above, it is necessary once and for all to lay down a rule that may not be tampered with; otherwise, we fail to eliminate the temptation of regarding wanted results in another light than un-desired ones. On this score also, *Fisher*'s view implies a return to the subjectiveness it was desired to avoid.

Among *R. A. Fisher*'s great achievements in statistics the most widely known is perhaps his method of analysis of variance. This method makes it possible to take into account several differences and their standard errors at the same time. The method is widely used in genetics, but much less so in medicine.

In principle *Fisher* proceeds from the following assumption. He compares the variability within the various subpopulations with the variability between them. If these variabilities are expressions of the same variability, if, in other words, the materials come from the same population, there must naturally be a definite ratio between

them. Obviously the means of the subpopulations must vary less than the individual values in the population since they are based on more determinations and therefore are more certain. The ratio between the variability within the subpopulations and the variability between the means of the subpopulations can be calculated if it is assumed that the subpopulations are chosen at random from the same population. If the means vary more, the subpopulations are, in other words, not taken from the same population and show a real difference. It may be said that the situation which is most frequent in medicine is a special case. There one only has one difference between two populations and its magnitude is compared with the variability inside the populations, as measured by the standard error of the mean. *Fisher*, here, does not use the standard error of the mean but σ^2. Of course, this cannot make any difference. As *Bonnier* and *Tedin* point out, exactly the same result is obtained on equal materials by the so-called classical method and by *Fisher*'s method.

In some quarters one seems to think that the classical method is wrong and that *Fisher*'s method is correct. This is the case only if it is a question of several differences, but not if you wish to compare two materials with only one difference between them. In most cases in medicine it is possible to use the classical method, the result of which is more easy to understand for the ordinary reader. It may, for example, be desirable to compare figures obtained for several years. In so doing there is nothing to prevent the materials from the various years from being added together to give a figure with a smaller standard error of the mean and which is directly comparable with the corresponding figure from a similarly treated control material.

Lastly a few words about *Fisher*'s way of using the square of the standard deviation which he calls "variance". This is quite confusing to an ordinary reader. The reason why *Fisher* uses this procedure is of course not that he wishes to avoid work by not having to extract the square root of a number, but simply that it is possible to add the variance of the subpopulations and the variance between them and thus obtain the variance of the entire material. The whole thing is based on *Pythagoras*' theorem stating that in a right angled triangle the sum of the squares on the smaller sides is equal to the square on the hypotenuse. The advantage gained hereby is, however, offset by the fact that the method becomes more difficult to under-

stand for ordinary readers. One merely gets rid of the paradox that the standard deviations added together are larger than their sum, which is due to the fact that sometimes the variability goes in the opposite direction and only sometimes can be summed up.

It seems surprising that *Fisher*'s views have been so widely accepted without giving rise to discussion. The explanation probably is that there is prevalent a strange respect for mathematicians and persons conversant with theoretical statistics. Obviously mathematicians are capable of making calculations and arriving at results impossible of attainment by ordinary people. Yet in performing his operations a mathematician uses a purely parrot-like and mechanical technique to which he has been trained, but he does not think. Naturally he must think when he creates new mathematics and works out new formulae. Evidently he must also do some thinking when he chooses the mathematical procedure which is best suited to solve a problem, but he does not need to think when he solves an equation of 2nd degree etc. Moreover, it is generally known that mathematicians sometimes are not especially intelligent when they tread new ground outside their own field, when it comes to politics and so on. However, it appears as though people's capacity for thinking became paralysed by mathematics and statistics. Sometimes, on the contrary, one takes a desperate step and says that all statistics is bunkum. In both cases one refrains from using one's common sense. Nevertheless, the better mathematicians and statisticians have no pretentions of being considered experts in all fields. Owing to the habit they get of working with exactitude, they on the contrary do not dare to express themselves on general subjects. Often they therefore seem colourless and impersonal as do persons who do not dare to have their own opinions. Amateurs in the field, however, often go to the other extreme. Owing to their insufficient knowledge, they overestimate the importance of what little they do know and hold forth with unreasonable pretensions. They express themselves as though they could solve every problem with mathematics and statistics and they undervalue work that does not have a lot of mathematics or statistics in it. It is the less well informed who quote the saying that they have no faith in anything short of actual measurement and the rule of three. *Fisher* has been so much in touch with biology that he has realised this danger and in one of his books he says a few words which are worth quoting in this connection.

"For it would be wrong to say that work with mathematical symbols requires greater intelligence than original biological work; on the contrary, the former may probably be likened to handling microscopes, staining liquids and the like. Original work in both fields demands similar qualifications of the intelligence."

Summary.

In statistics it is generally assumed that a difference three times greater than its standard error can be taken as significant. Some English and American authors, however, are content with two times the standard error. The problem is therefore discussed here.

Resumé.

En statistique, on considère en général un écart comme significatif lorsqu'il est le triple de l'erreur moyenne. Les auteurs anglais et américains se contentent d'un écart qui n'est que le double de l'erreur moyenne. Ce problème est discuté en détails.

Zusammenfassung.

In der Statistik betrachtet man im allgemeinen einen Unterschied, der sich auf die dreifache Größe des Mittelfehlers beläuft, als sichergestellt. Ein Teil englischer und amerikanischer Verfasser begnügt sich indessen mit einem Unterschied, der sich auf die zweifache Größe des Mittelfehlers beläuft. Deswegen wird dieses Problem diskutiert.

THE PROGNOSIS OF DISEASE

by GUNNAR DAHLBERG
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It is important for a practising doctor to be able to tell his patient how things will go with him. One of the reasons why he goes to the doctor is that he is anxious. He wants to know whether he is likely to get well again and how long his illness will last. Perhaps he has to arrange for a longer or shorter period of absence from work. Nowadays doctors have a general idea of the prognosis of most illnesses. They can, with certain reservations, give information of some value. However, there are exceptions to all rules. One must therefore always point out that the unexpected may happen and that an illness, which is usually neither very serious nor long drawn out, may take an unfavourable turn. Conversely, when the illness is serious, one must say that "while there is life there is hope", and that the illness may unexpectedly take a turn for the better. If the patient presses the doctor and demands more definite information the doctor has often not much to give, as we have no very exact knowledge of the prognosis of most diseases.

We fairly well know the risk of death immediately after falling ill. It is when it comes to the prospect of getting well in the long run after leaving the hospital that our knowledge is more scanty. We wish to have more definite information about the prospects of getting restored to health to a different degree after leaving the hospital. The difffculty is greater in this case than one should expect, because it is not very easy to have information about patients after they have left the hospital. This is especially so in counties where the population is moving about very much and where the registration is not good. The object of this paper is to discuss some of these difficulties.

Of course the cases should be divided up according to age and sex. The final figures should be obtained through statistical analysis

but it is also necessary to ask the advice of a statistician when beginning the investigation. Otherwise important points may be missed. The material will be incorrectly assembled and necessary data will be lacking. Later on, when the material is to be worked up statistically, it will either be too late to fill in the gaps, or else it is necessary to go back and supplement the information which was collected and this is both timeconsuming and expensive. If the questionary had been better planned in the first place it would have been easy to obtain a useful material without a significant increase in the work of collection. In any case it is necessary to have definite and clearly defined limits when dividing up the material into classes of people who get quite well, who still have symptoms of the disease and people who are more or less restored to health, so that they are able to work to a certain extent and so on.

The first question which presents itself is how large a material is required. It is impossible to give a general answer to such a question. Of course, other things being equal, the larger the material the better. The errors diminish as the material becomes larger, so that the figures become more exact. However, it is always necessary to limit the material for practical reasons. Even a small series is of interest in cases where our knowledge of the prognosis of the disease in question is very vague. When a common disease is to be studied a larger series is usually required than where the illness in question is rare. Such investigations often deal with the prognosis of a special type of case, for example cases occurring in the aged, cases treated in a certain way, cases where some particular complication has arisen etc. It is then necessary to obtain a control series for comparison. If the work of collecting both series is equally great the control series should be as large as the one investigated. Special precautions may be required to ensure that the series are comparable.

Although no general advice can be given as to the planning of an investigation one can point out certain mistakes which are commonly made by the "normal person". In beginning to collect such a series people generally start with cases admitted to a hospital for that disease for the first time during a certain period. Perhaps the series is not as large as was expected, and the investigator tries to augment the material by including all cases of the disease which were in the hospital during the period. However, he notes the date of onset of the disease in such patients and their previous symptoms.

Thus, formally speaking, all the cases have been followed up from their onset. Such a series of course gives rise to erroneous figures.

When investigating schizophrenia for example one must not include patients already in hospital and only new admissions can be used. Supposing, for example, one were to investigate patients falling ill between 1920–25 one would be on the safe side. However, if one were to include patients already in hospital the figures obtained for the prognosis would be far too pessimistic. A patient who was in hospital between 1920 and 1925, but who first became ill in 1909 and was then admitted to the hospital is not a randomly selected case. Many people fell ill with schizophrenia in 1909, but some got well again and were discharged from the hospital. A patient who is still in the hospital is a selected case having a bad prognosis. Thus patients still in hospital are, to some extent, selected cases having a weak power of recovery. An altogether too pessimistic view of the situation is obtained by combining new and old cases in this way. *Stenberg* (1948) is the only worker who has taken this source of error into account and investigated the prognosis of schizophrenia correctly. 30 odd authors, using series of various sizes, have previously tried to cast light on the prognosis of schizophrenia, and all have gone astray. The most important factor in this connection is that, as *Stenberg* showed, the tendency to recover is greatest during the period immediately after admission. The patients who remain in hospital form a group which lowers the figures for the percentage of cases recovering. *Stenberg* was thus able to show that the outlook in schizophrenia is much brighter than was formerly supposed. The investigation has become of special topical interest owing to the introduction of shock therapy. Comparative figures are required in order to determine the extent to which the treatment improves the prospect of recovery in comparison with the prospect of spontaneous recovery. It should be mentioned, for the sake of completeness, that there is nothing to prevent one from using patients already in hospital from the time when the investigation begins, that is to say from the time when the patient will be included in the investigation whether he recovers or not. When presenting a series of cases one must always give the date on which the follow-up investigations began and ended. In other words, one should never carry one's investigations backwards in time even when records can be made formally in such a way that it appears as though the case had been followed forwards. One must avoid every selective factor influencing the prognosis.

Another difficulty which is often encountered concerns series where some of the patients have received a particular form of treatment. We will take the statistics for cancer as an example of this. Let us assume that we wish to investigate the prognosis for patients suffering from cancer of a particular organ. We may assume that all untreated patients will die. If some recover this must be attributed to a false diagnosis. Investigations of the prognosis for untreated cases can only be concerned with determining how long a cancer patient can live, which is naturally not without a certain interest.

Now let us consider the cases who receive a particular form of treatment. The proportion of cases receiving surgical or radiological treatment or both depends on two factors. First on the greater or less tendency of the patients to consult a doctor in the early stages of the disease. And secondly on the strictness of the indications required for treatment by a particular method. It stands to reason that, in a country where the level of medical knowledge among the public is low, or where people have little faith in doctors and hospitals, many of the patients will not consult a doctor until the disease is too far advanced for him to be able to do anything about it. It is furthermore clear that hospitals and doctors who are very cautious in their indications for treatment will have a good statistical record. They treat comparatively few patients but seldom have a recurrence. A doctor applying wider indications for treatment will have a poor statistical record, but be may save the lives of more patients. If I remember rightly Dr. *Hjalmar Forssner* revealed a dramatic contemporary example of this state of affairs. He showed that a French hospital, which had a remarkably low mortality among eclamptics treated by *Stroganoff*'s method turned away all the more severe cases. Their facilities were poor so they only undertook the treatment of mild cases. It was not surprising that the results of the treatment were striking.

It is also obvious that one must try to include all cases when assembling a series of cancer cases. One can then calculate the statistical prognosis of those who received treatment and note how large a proportion this makes of those who sought care, or more correctly, of those who consulted a doctor. One thus obtains certain criteria for judging the state of affairs. However this is not enough. One must also take the circumstance mentioned above into account, namely that people consult their doctors at different stages of the

disease in different times. A general alteration in the direction of consulting the doctor earlier will mean that a higher proportion of cases will receive treatment and the all-round prognosis will be better. One must therefore try to obtain some information as to the stage of the disease at the time when the patient consulted the doctor. One can sometimes derive some information on this subject from the interval between the onset of the first symptom and the first medical consultation.

A supplementary method of approach to the problem is to try to determine the degree of extension of the cancerous process at the time of treatment and thus to classify the patients according to the stages of the disease, which are more or less well defined. This was the method of approach attempted in the statistical record of cancer cases which the League of Nations tried to compile. Naturally it is not easy to obtain objective criteria for the degree of extension of the process. One cannot rely on different doctors in different countries and with different training using the same classification in their clinical practice. It therefore seems to me that one ought always to supplement statistics based on classification according to stages of the disease with information as to the interval between the onset of the first symptom and the beginning of treatment. It is not, however, always easy to decide exactly when the first symptom appeared. One can then try to record the cases in such a way that one can assess the earliest and latest time at which the first symptom could have appeared according to the case history.

The method of recording the material must further be modified in accordance with the nature and course of the disease. The problem is often very hard to solve. It is specially desirable to carry out investigations of as objective a nature as possible using methods which are statistically sound, when dealing with cases requiring treatment by surgery or by other means which carry an immediate mortality. One reason for this is that there is a danger that a deep rooted faith in some method of treatment which is not in fact beneficial to the patient may persist for decades or more if one does not make use of such means as exist for checking the results of the treatment, even though these means are often but small. *Robin Fåhraeus* pointed out a specially instructive example, namely that for thousands of years the practice of blood-letting for pneumonia meant that the doctors killed considerably more patients than the

illness. According to the statistics compiled by the Viennese doctor *Dietl* which are the best available, four times as many deaths occurred among those who had been bled as among those who had not. *Fåhraeus* (1944) expresses the matter thus: "They thought it was the illness that was being done in by blood-letting but in fact it was the patient who was being done in."

Finally, we wish to mention the curious error which may arise when trying to compute the death-rate of accidental cases. In a work on skull injuries Dr. *Johan Cedermark* points out that the mortality in the hours immediately following the accident depends on the area served by the hospital and the state of communications. If it takes a long time to bring the patient to hospital he may die on the way and never be admitted and thus not be included in the material. The material is thus selected to some extent. This should be taken into account if figures for mortality at various times after accidents are being drawn up.

I can be brief in my discussion of the working up of the material. The time of the last observation must be recorded, i. e. the last chance of getting information as to the patient's condition. The different periods of observation are used in the statistical compilation and are related to the number of deaths, recoveries, improvements etc. occurring within the same period of observation. The working up is laborious and somewhat complicated and can scarcely be carried out except by a staff of trained statisticians. The details of this work are therefore hardly of great general interest.

I will close with a few words on the choice of material. If one uses a series of cases treated a long time ago one will obviously be able to use long periods of observation and can therefore make a statement as to the long-term course of the disease. However, the disadvantage is that the information is often incomplete in some respects. X-Rays and other clinical methods such as are now used for making a diagnosis, were not available in the past. If, on the other hand, one uses recent material, the period of observation is short and one cannot find out how the patient will get on in the long run. Of course the diagnosis is more reliable and the material can be used for a more detailed analysis of the symptomatology of the onset of the disease and the immediate effect of treatment. If possible it is best to use both approaches and investigate both an old and a recent series. The investigations will then complement

one another and provide an opportunity for comparing the series in respect of such problems as symptomatology, the reliability of the diagnosis etc.

Summary.

The method of computing the chances of recovery in different diseases, i. e. the prognosis, is discussed. Some more common types of error are pointed out.

Résumé.

La possibilité de calculer les chances de guérison, c'est à dire le pronostic, est discutée. L'auteur attire l'attention sur les erreurs habituelles.

Zusammenfassung.

Die Möglichkeiten, die Genesungs-Aussichten bei verschiedenen Krankheiten zu berechnen, d. h. die Prognose, wird diskutiert. Der Verfasser hebt einen Teil gewöhnlicher Fehlerquellen hervor.

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VENEREAL DISEASE AND PROSTITUTION

by GUNNAR DAHLBERG

With respect to their sexual behaviour in society, women may be divided into a few different groups.

Some are monogamous and some are more or less polygamous. The extreme cases are a married woman who is absolutely faithful and a professional prostitute who accepts sexual intercourse with anybody who is willing to pay. Roughly speaking, women may be divided into three groups: 1. married and largely monogamous women, 2. slightly polygamous women and amateur prostitutes who have sexual intercourse with several men but who do not play their trade professionally, and 3. professional prostitutes. If venereal diseases are considered solely from the point of view of contagion, the above classification appears to be fully satisfactory.

No exact data are available as to the rôle played by prostitutes as propagators of venereal diseases. However, the opinion commonly held would seem to be that they play a most important part. This appears to be true, judging by the fact that the incidence of venereal disease is greatest in metropolitan areas where the prerequisites for prostitution are present. In this connection we shall digress temporarily and discuss the economic aspects of prostitution.

The current price of sexual intercourse with a woman naturally depends on demand on the one hand and on the supply of prostitutes on the other. When economic conditions are good the demand increases and the price goes up. The primary result of the increased demand is that the number of coitions per prostitute becomes greater. Consequently, the nightly earnings increase and, therefore, the recruitment to the profession may also be expected to increase. When times are bad and money is scarce one may perhaps expect the demand to slacken, but not so much as one perhaps would be inclined to think. We shall return to this question later. But in critical times one may also expect that women will have greater difficulties in making both ends meet, and that, consequently, more of them will be forced to become professional prostitutes. It is likely that quasi-

21*

prostitutes with a job will be the first to be dismissed when times grow worse and that these then will be forced into full-time professional prostitution.

If measures taken by the authorities reduce the number of prostitutes, the effect will be similar. The frequency of coitions per prostitute will increase if their number decrease as long as the demand remains constant. The result will be a rising price level and more numerous recruitment to the trade. In other words, this price increase counteracts the steps taken by the police. If the measures cause the price to go up very significantly, the demand can, however, be expected to go down somewhat. Nevertheless, in this respect there very likely is a considerable price tolerance or, to use a term from economics, a small price elasticity, much like the situation that has been demonstrated to exist as regards alcohol. When the government increases the price of alcohol, the demand does not decrease as much as might be expected. At most, that part of the public which has used better brands of spirits will revert to cheaper ones. It is often remarked that alcohol cannot become too expensive and that it always is worth its price. There is in other words a broad latitude within which price increases have no appreciable effect. So, it may be assumed that persons who desire sexual intercourse with prostitutes are not very susceptible to raised prices. The demand is especially marked in persons with strong sexual cravings and such as cannot satisfy them by any other means. It may therefore be assumed that particularly persons who are in some way disabled or otherwise have a repellent appearance and, further, persons who are old and must therefore take recourse to prostitutes will form a small vanguard among the customers at large. Most of the remaining demand may be expected to derive from youngish bachelors. This is a natural result of the late marriages and is therefore an unavoidable feature of present-day civilization. The hopelessness of attempting to eradicate prostitution is mainly due to these factors. The steps taken merely increase the price but have hardly any effect on the frequency of sexual intercourse with prostitutes.

We shall now pass on to the relationship between the incidence of venereal disease and different degrees of polygamy. If every man kept to one woman and vice versa, the venereal diseases would obviously disappear at once. They can only be propagated when men and women are being to some extent promiscuous. Actually, the number of men who become diseased must in their turn infect an

equal number of women with the same degree of promiscuity as the women who caught the disease in the first place. If this balance becomes disturbed, one must get aberrations that are comparatively strong since the "generations" of diseased follow in fairly quick succession. The relatively constant incidence of the venereal diseases indicates that in this respect there are no appreciable aberrations. However, the aberrations that do exist may, of course, also be due to propagational changes even if the frequency of coitions, which in this respect is of the greatest importance, remains unchanged. We shall therefore in the following discuss the incidence of the different venereal diseases separately. However, before so doing, it should be recalled that by means of the numerical proportion between the sexes certain conclusions may be drawn as to the method of propagation of the venereal diseases. If each of a given number of polygamous women transfer the disease to a large number of men, say 10, and the disease goes no farther, it may be called an effect of the first degree. In such cases it is characteristic that women are in minority among the diseased. If the diseased men in their turn pass on the illness, it is likely that they will do so to their wives, if any, or to other corresponding persons with whom they carry on a more constant relationship. The disease may then be called an effect of the second degree. Then the frequency of the women will approach fifty per cent. Ulcus molle seems to be an effect of the first degree, syphilis of the second degree, while gonorrhea seems to have an intermediary position. (Cf. *Dahlberg*, 1941). In the above reasoning we have schematically distinguished only between monogamous and polygamous women, paying no regard to the existence of various degrees of polygamous habits.

Venereal Diseases in Sweden.

In our country we have figures for the incidence of the venereal diseases throughout the country as from July 1st 1912, i. e. from and including the year 1913. Before this date the figures we have refer only to persons who received hospital treatment, and, naturally, these figures cannot give a true picture of the incidence of the respective venereal diseases. A survey of the incidence of venereal diseases after 1912 is offered in the appended diagram. In it the logarithmic scale is used vertically. By this means a better picture will be had of the mutual increase and decrease, respectively, of the venereal diseases.
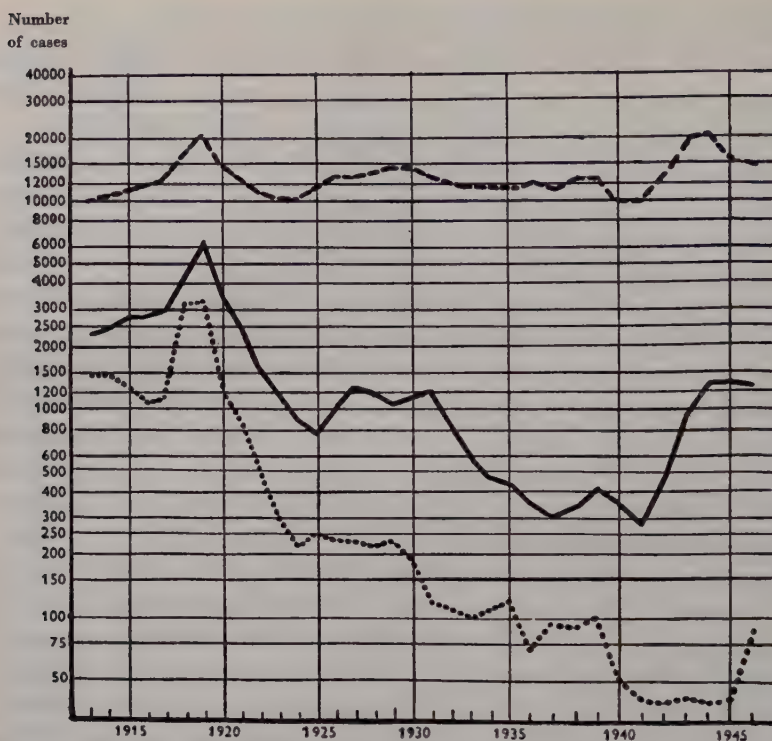
Fig. 1. Number of cases of gonorrhea (broken line), syphilis (whole line), and ulcus
       molle (dotted line) in Sweden 1913–1946. (Semi-logarithmic scale.)

We see that before the first World War, ulcus molle seems to
have had an incidence of close to 1.500 cases annually. During the war
the frequency went up to slightly more than 3.000 cases in the years
1918 and 1919. Then the frequency rapidly dropped considerably
below the prewar one. In 1924 there were 215 instances of ulcus molle.
From then onwards the incidence dropped still more, so that in recent
years the disease may be regarded as being practically extinct. How-
ever, it will be observed that there was a slight increase in the fat
years before 1930 and towards the end of the second World War.

With respect to syphilis the picture is similar in principle, i.e. an
increase to more than 6.000 cases during the first World War, then
a drop which turned into an unimportant increase in the years before
1930, and then a new decrease. The lowest figure was attained in 1941
with 273 cases. Then, towards the end of the second World War, there

was a new increase which was marked but more moderate than during the previous World War, viz. to 1.300 cases.

Common to both these diseases is their on the whole downward trend in frequency. With regard to syphilis it is often maintained that this is due to improved methods of treatment. The downward tendency of ulcus molle cannot have a similar explanation, however. Actually the diseases run so parallel that one looks for a common reason for their lower frequency. Therefore one cannot with certainty state that the treatment has had a greater effect on the frequency of syphilis.

Coming finally to gonorrhea, we find that as for the other venereal diseases there is an increase which seems almost to double its incidence during the first World War. We then get a new increase prior to 1930 and yet another increase during the second World War with its maximum in 1943. Then the top was approximately on level with that during the first World War.

What is of particular interest in this connection is the proportion between men and women among the sufferers from venereal disease. (See fig. 2). For ulcus molle we find an increased proportion of women during the raised frequency in the first World War. Then the relative number of women drops more moderately and later it seems to be practically unchanged. The figures, however, show great irregularities owing to the small number of cases. Possibly an augmented proportion of women may be recorded towards the end of the period of increased frequency at that time.

We also have an increased proportion of syphilitic women during the raised frequency in the first World War. Thereafter, the proportion of women goes down but largely it seems to have increased up to the present time. This is especially the case during the last part of the second World War at which time the disease became more common. Also for this disorder the figures are rather irregular, which is due to the fact that the number of cases is so small.

We get a more reliable conception of the situation when we are dealing with gonorrhea, since this disease is more common. Here also we find a transient increase of the proportion of women during the period of higher incidence in the first World War. When this maximum has levelled off, we obtain a fairly regular increase of the sexual proportion up to the present time. It should be emphasized that during the first World War the proportion of women was 26 per cent, i.e. for every woman there were about 3 diseased men. During the
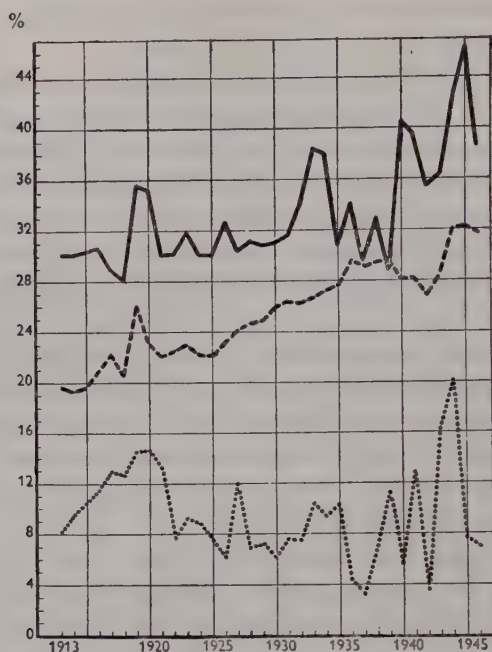
Fig. 2. Percentage of women among persons with syphilis (whole line), gonorrhea
(broken line), and ulcus molle (dotted line) in Sweden 1913–46.

period of increased incidence during the second World War 32 per cent
of the diseased were women. Although at this time the disease was
about as frequent, every diseased woman in other words corresponded
to about 2 diseased men. These circumstances indicate an essential
change in the propagational mechanism of the disease. The fact that
a venereal disease is sustained by a low percentage of women must
be due to its mainly being limited to professional prostitutes or highly
polygamous women and men. This seems to be the case as regards
ulcus molle. As regards syphilis, on the other hand, the fact of the
matter seems to be that women become diseased as often as men,
indicating that it is not confined to extremely polygamous persons
and that it is relatively frequent also in women and men who are not
so highly polygamous. With respect to the sexual proportion gonor-
rhea takes an intermediary position. The essential thing is that for
gonorrhea the situation has changed, and that a larger proportion
of women become diseased. Primarily one is inclined to think that

successively up to the present day professional prostitutes play a less important part in the propagation of the disease than was the case in bygone days. A similar change may perhaps also be noted as regards the other two venereal diseases, but less certainly because of the smaller number of cases.

Prostitutes in Sweden.

Under such circumstances there is reason to enlarge somewhat upon the importance of professional prostitutes in the propagation of venereal diseases. Far and away the best source of knowledge about prostitution in Sweden is the publication issued by the so called Committee on Reglementation and, above all, the investigations made in connection therewith by Professor *Jöns Johansson*. His statistical treatment of the available material is exemplary in many ways. The most important question from medical points of view, viz. the role played by prostitutes in the propagation of venereal diseases, was unfortunately not studied, however. So far as I have been able to find this matter is touched upon only in a footnote, citing figures from Doctor *Müllern-Aspegren*'s private practice. He had systematic-ally asked his patients how they had caught the disease. A specified answer could not be given by 60 per cent. Half of the remainder had received the disease from registered prostitutes, the rest from others. Of course the statement is not much to base an argument on. Sup-posing that the unknowns are distributed in the same manner, one could risk the statement that the prostitutes in Stockholm were res-ponsible for half the cases of venereal disease. The unknown are, however, far too numerous for such an interpolation to be defensible.

The legal prostitution was as we know abolished in 1918 by the passing of the bill termed Lex veneris. However, in a manner of speaking, the so called Vagrancy Act has done the service of the reglementation rules. It has enabled the police to deal with prostitutes and admonish them or sentence them to forced labour. It may be said that by the Vagrancy Act the worst aspects of the Reglementation Act were retained. The only thing that actually was abolished was the medical supervision which surely was to some purpose. The possibility of interference on the part of the police remained, however, which from medical points of view appears to be comparatively irrational. To admonish prostitutes is naturally of no avail whatever, and to sentence a small number to forced labour is probably of equally small importance, since the majority of prostitutes still are tolerated. At

the turn of the century their number in Stockholm, according to
J. Johansson, was slightly less than 1.000 which is equivalent to a
little more than 1 prostitute per 100 unmarried men. (He did not
calculate the number of married men per prostitute). However, in
1932 the number of women admonished for vagrancy was 109 and in
1939 it was 70. Provided that the number of professional prostitutes
has kept more or less in step with the growth of the city (the popu-
lation of Stockholm has approximately doubled since 1900), it is in
other words but a small proportion who have been admonished. The
number sentenced to forced labour is naturally even smaller.

Table 1. Syphilis and gonorrhea among new inmates at Landskrona
Institution of Forced Labour in the periods 1921–1931 and 1933–1938.

New inmates at Landskrona	No. of cases	Percentage of new inmates
Period 1921–1931:		
Number of new inmates	1.395	
No. of cases of syphilis	989	70.9
of which with symptoms.	48	3.4
No. of cases of gonorrhea	53	3.8
Period 1933–1938:		
No. of new inmates	445	
No. of cases with syphilis	302	67.9
of which "with symptoms" in stages I and II .	7	1.6
No. of cases of gonorrhea	35	7.9

In order to obtain some idea of the extent to which those who
qualify under the Vagrancy Act are contagious one may investigate
how many have been registered as being diseased when they com-
menced their forced labour. Data on this subject is published in the
annual reports of the Institution of Forced Labour for women at
Landskrona. The result of such a study is given in table 1. It may be
surmised that those sentenced to forced labour, if anything, are more
disorderly than the average of this type of woman and that the above
figures, consequently, are too high rather than too tow.

Figures are given for two periods, partly the 11-year period 1921–
1931 and partly the 6-year period 1933–1938. As the average number
of internees is lower in the latter period, it is likely that, at that time,
the selection was somewhat more stringent. However, the two sets
of figures are not significantly different.

It will be seen from table 1 that about 70 per cent of the women have syphilis. Since some of the internees are young and have not plied the trade of the prostitute for so long, it is natural that some are not diseased. Nevertheless, the high figure shows that the professional prostitute, if she remains in the profession for any length of time, practically always becomes diseased. After another few years she naturally becomes resistant to infection. From this point of view it may be said that elderly professional prostitutes may be regarded as absolutely free from risk. During the first period it was only 3.4 per cent who exhibited symptoms, and, of course, some of these may not be contagious, as the symptoms may very well have been of the tertiary type. During the second period one has distinguished between the various stages. It appears that merely 1.6 per cent are in stages I and II, and at least periodically these must be regarded as being contagious. But as syphilis, which is pointed out above, is fairly infrequent in Sweden, it is possible that the prostitutes are sufficiently numerous to be responsible for the cases of syphilis among men. Naturally, some of the cases of syphilis among women must be caused secondarily by the men. In some cases it should be a question of married or monogamous women who do not pass the disease on further.

Coming now to the figures for gonorrhea, we obtain for the whole of the period 1921–1938 the low percentage 4.78. That it is higher in the latter period and lower in the former may be due to random variation. Now it does seem rather improbable that this low frequency should have the greatest importance for the propagation of gonorrhea. If prostitutes were the main instruments a far higher figure should be expected. If we assume that there are 2.000 professional prostitutes in Stockholm only about 100 of them would be contagious, provided that the above percentage is considered representative. It seems unlikely that this number of contagious prostitutes could be responsible for the majority of cases of gonorrhea among men in Stockholm.

No cases of ulcus molle have been recorded for the women sentenced to forced labour. Most likely only solitary cases have occurred. Lastly, it may be pointed out that as a rule the internees do not arrive at the institution for forced labour until about a week after the police have detained them. Therefore, it is hardly conceivable that any of them may have been subjected to treatment and have recovered after the detention by the police before the arrival at the institution.

In synopsis it may consequently be stated that the available data as to the incidence of gonorrhea in women sentenced to forced labour hardly suggest that such women are the main instruments in the propagation of the disease. The up to the present time increasingly greater number of women among the diseased persons also suggests that professional prostitutes do not play the most important part in the propagation of the disease, but that the amateurs in the field are more dangerous. In regard to syphilis, it is possible that the same process is rampant but the numerical material is too small to permit the drawing of any more definite conclusions. The same applies to ulcus molle. The latter disease is to all intents and purposes extinct and the cases that do occur most likely accrue from sailors and from persons who have been abroad and infect individual prostitutes, thereby giving rise to a minor local epidemic.

% respectively per 100 000 inh.
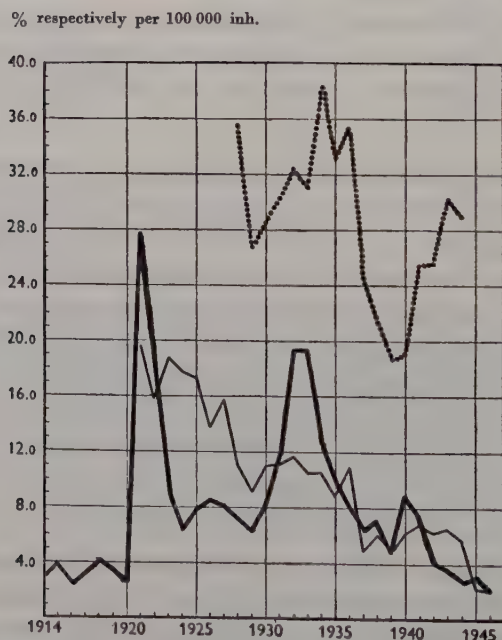
Fig. 3. Per cent unemployed of the members of the Trade Unions 31.1.1914—31.7.1946 (thick whole line), number of women detained for vagrancy per 100 000 of the population (thick dotted line), and number of women admonished for vagrancy (thin whole line) per 100 000 of the population.

With regard to the number of prostitutes there are no data for recent decades. If the police detained and admonished a constant percentage of prostitutes under the Vagrancy Act, this number would give some idea of the frequency. It is possible, however, that the police has modified its principles. With this in view, the statements made in the following must be accepted with some reservation.

We have pointed out that the number of prostitutes should increase in good times as well as in bad. In the former case the greater earnings is the incitement to join the corps. In figure 3, curves are given partly for the unemployment according to *Dahlberg-Tingsten*, and partly for the number of detained and admonished women. It will be seen from this figure that unemployment has no decisive effect on the course of the curves for vagrancy. Those detained increase in numbers some years after the maximum of unemployment, and also during the second World War when there were very few unemployed. Obviously, therefore, factors other than the state of business and finance influence the frequency of measures of the police against the prostitutes.
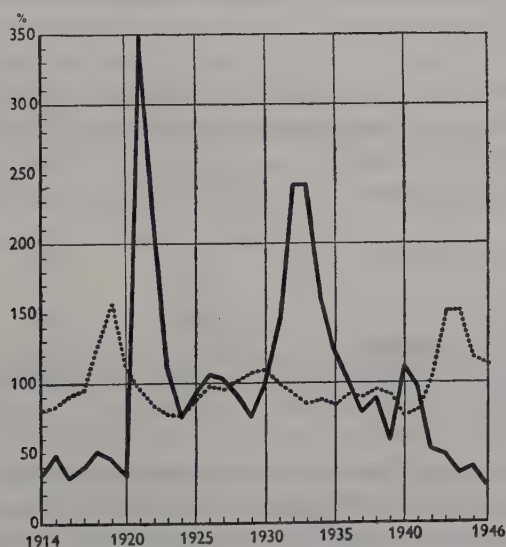
Fig. 4. Unemployed every year in per cent of the total number of unemployed during the whole period 1914–1926 (whole line), and cases of gonorrhea every year in per cent of the total number of cases of gonorrhea during the whole period (dotted line).

It may perhaps also be interesting to see to what extent the incidence of venereal disease is parallelled by unemployment. A survey of the situation in respect to this is given in fig. 4. On the whole one gets a distinct impression that the venereal diseases become more prevalent as unemployment decreases and vice versa even if the connection does not seem to be a very marked one. This suggests that such diseases in a measure are influenced by economic conditions, at any rate more than the number of prostitutes who are dealt with under the Vagrancy Act.

These two curves show indirectly that the incidence of gonorrhea remains unaffected by the number of prostitutes, at least so far as one can judge by the number who are dealt with under the Vagrancy Act.

Figures have been published for the number of internees who were infected with venereal disease at the time of their "admittance to the institution" in an investigation performed by the Board of Social Welfare and which comprises persons admitted to Landskrona from the beginning of 1916 to the first half of 1924 inclusive. It is emphasized that the great majority probably are full-time professional prostitutes. The result of this investigation is given in table 2. It appears

Table 2. Incidence of venereal diseases in women sentenced to forced labour at Landskrona in the period 1916–1924.

No. of inmates having	No. of cases (excl. cases with data mising)	Percentage	Percent of all 936 cases including cases with missing data
Both syphilis and gonorrhea	325	38.9	34.7
Syphilis only.	273	32.7	29.2
Gonorrhea only	150	18.0	16.0
Neither syphilis nor gonorrhea . .	87	10.4	9.3
Total no. of cases.	835	100.0	89.2

from the table that 72 per cent of the women were infected with syphilis and 57 per cent with gonorrhea. The latter figure is evidently essentially higher than the one in our material and would seem to suggest that formerly professional prostitutes were much more frequently contagious than they are now. The difference is so striking that if the figures of the Board of Social Welfare actually refer to the time of admittance to the institution, it could be regarded as absolutely cer-

tain that nowadays prostitutes play a significantly less important role than formerly. However, the difference seems to be so large that I doubt that the Board's figures refer only to the time stated. It is remarkable that no data are supplied for ulcus molle. Even if it is certain that the figures for women sentenced to forced labour formerly might have been somewhat unreliable, the difference, nevertheless, is so large between the different periods that some change must have taken place. It is remarkable that those who have had both syphilis and gonorrhea amounted to 38.9 per cent during the period 1916–1924. The corresponding figure for the period 1921–1931 is only 1.43 per cent, and after 1931 no figures are given. The significantly higher figures for the coincidence of syphilis and gonorrhea indicate that formerly venereal diseases were much more prevalent among the prostitutes than in recent times. Perhaps it is most likely that the change with respect to gonorrhea has to do with the fact that contraceptive measures have become more common and that particularly the prostitutes understand better how to protect themselves. It is conceivable, therefore, that nowadays the amateurs in the field, who do not employ contraceptive agents so frequently, are of greater importance to the propagation of venereal diseases and that, from this point of view, countermeasures against the prostitutes appear to be still more meaningless than before. Prostitutes who are intoxicated or otherwise disorderly should naturally be taken care of by the police, but the police can very well do so without resorting to the Vagrancy Act and thereby have them sentenced to years of forced labour. A penalty of this kind cannot very well have any improving effect, rather the opposite.

Summary.

In an earlier paper (*Dahlberg* 1941) the author has discussed the proportion of women, respectively men, among the cases of venereal diseases. The important thing from this point of view in this paper is that the sexual proportion is different when the professional prostitutes are the main cause of the cases of the disease in question and when they play a more insignificant role. It is shown that the proportion of diseased women in Sweden increases up to the present time which seems to indicate that the amateurs, not the professional prostitutes, begin to play a greater role. Some facts are then given about the venereal diseases of the professional prostitutes.

Résumé.

Dans un précédent travail (*Dahlberg* 1941) l'auteur a discuté la proportion de femmes et d'hommes parmi les cas d'affections vénériennes. Il ressort du présent travail que la proportion des sexes est différente lorsque les cas de l'affection considérée sont principalement provoqués par des prostituées professionnelles ou lorsque ces dernières jouent un rôle plus insignifiant. L'auteur montre que la proportion des femmes atteintes en Suède augmente progressivement, ce qui semble indiquer que les prostituées amateurs et non les professionnelles commencent à jouer un rôle plus important. Il cite ensuite quelques faits concernant les affections vénériennes chez les prostituées professionnelles.

Zusammenfassung.

Der Verfasser hat bei früherer Gelegenheit (*Dahlberg* 1941) das Zahlenverhältnis zwischen Männern und Frauen bei Fällen mit venerischen Krankheiten diskutiert. In der vorliegenden Arbeit ist ein wichtiger Faktor von diesem Gesichtspunkt aus der, daß die Verteilung nach dem Geschlecht verschieden ist, wenn die Berufsprostituierten eine wesentliche Ursache der Fälle mit genannter Krankheit ausmachen und wenn sie eine mehr unbedeutende Rolle spielen. Es wird gezeigt, daß die Anzahl geschlechtskranker Frauen in Schweden bis in die Gegenwart proportionell steigt; dies scheint anzudeuten, daß die Amateure, nicht die Berufsprostituierten, eine größere Rolle zu spielen beginnen. – Außerdem werden einige Fakten über Geschlechtskrankheiten bei Berufsprostituierten gegeben.

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OBESITY AND DIABETES

by GUNNAR DAHLBERG

Introduction.

Physicians have long had the impression that obese people comparatively often get diabetes, and their impression is confirmed by wholly satisfactory statistics. One interpretation of this is that people who eat a lot and therefore become fat damage their pancreas so that its function sooner or later may become impaired. Theoretically, one would expect that persons who consume much carbohydrates should strain their pancreas and therefore become diabetic, and that a diet rich in fats actually would be slightly protective against diabetes. If it were a fact that a diet consisting predominantly of fats caused or promoted diabetes, this would mean that diabetics previously were so managed that their condition was worsened. Since, however, insulin at that time was not available, the treatment was to some extent enforced by the disease.

Furthermore, it is generally so that an improved standard of living increases the consumption of fat. Accordingly one should be paying for the improved standard of living with an increased risk of getting diabetes. In other words the problem of obesity and diabetes is a very important one. The relationship between obesity and diabetes has been studied partly by animal experiments and partly by statistical analysis of figures for the mortality of diabetics. We shall discuss the latter questions first.

According to the theory mentioned above, the number of persons who become ill with diabetes should increase when the diet is richer in fats and decrease when the diet becomes richer in carbohydrates and proteins. In other words, the frequency of new cases of diabetes would be smaller during wartime when foodstuffs are rationed.

The Frequency of New Cases of Diabetes.

Unfortunately there are no statistical figures available for the frequency of new cases of diabetes. Theoretically, it would be possible to collect figures for the number of patients from a certain

population who annually apply for the first time to physicians, and thereby obtain frequencies that ought to agree fairly well with the number of new cases. However, the figures cannot be absolutely exact, as one cannot tell how long the person concerned has had the disease when he sees his doctor and because those who never see a doctor naturally cannot be included. Such figures not being available, however, it is not very fruitful to discuss this possibility.

The Frequency of Diabetes.

One has, nevertheless, been able to obtain some data as to the number of diabetics in the population. When rationing became necessary during the second World War, extra allowances of food-stuffs were usually given to diabetics. Therefore the large majority of those who suffered from this disease applied to the rationing authorities, and this made it possible to obtain fairly reliable figures for their numbers. Such data were collected in Sweden and in Switzerland. Swedish data were published in a paper by *Dahlberg, Jorpes, Kallner* and *Lichtenstein* (1947). The frequency of diabetes turned out to vary considerably between different age classes. Among young people the disease was not so common, but after about 40 years of age its frequency started to increase in both men and women. (The disease is between 9 and 10 times as common at 65 to 70 years as at 35 to 40 years.) Moreover, it appeared to be more common in cities than in villages and least common in purely rural areas.

The number of recorded cases of diabetes must now depend on: 1. to what extent the disease becomes known; 2. how long the diseased persons live after the onset of the disease, and 3. the proportion of the diabetics who avail themselves of the possibility of getting an extra allowance. A rural population will naturally be far less affected by food rationing than an urban population. It simply does not need extra allowances to the same extent. Therefore it is natural that the frequency of diabetics found is lower in rural districts. The fact that the disease apparently is more common in cities than on the land probably also is due to less complete knowledge of it among the rural population: in the country physicians are not plentiful, etc. That the number of diabetics should increase with age is also natural, because nowadays the death risk is not so great for younger persons. These will in other words survive to more advanced ages. However,

it seems improbable that the increase with age should be due to this accumulation only. Possibly it may be surmised that the strong increase in frequency in the higher age groups is attributable to a correlation between arteriosclerosis and diabetes. However, this question will not be discussed here in detail. I merely wish to point out the possibility and may later take up the problem in another paper.

With the object of illustrating the occurrence of the disease at various ages, a diagram is given of conditions in Stockholm. We have taken great pains to procure as reliable figures as possible for this city (fig. 1).
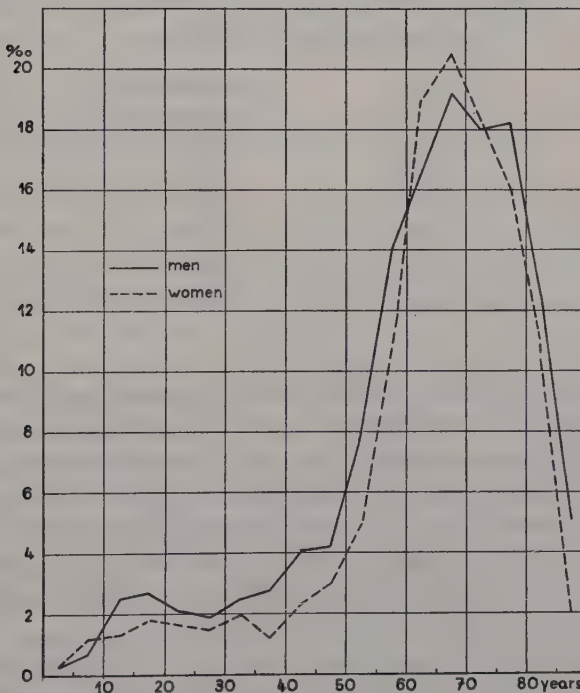
Fig. 1. Frequency of diabetics in different ages ———— Men   – – – – Women

It will be seen from the diagram that if we have two populations with the same risk for diabetes in the separate age groups but with different age distribution, then the frequency of diabetes will be

22*

dissimilar in these two populations. Figures for the frequency of diabetes in whole populations must therefore be regarded with caution. Strictly speaking, such figures for different populations are not directly comparable.

During recent years the official statistics have included figures for the number of diabetics at conscription. These figures are given in table 1. It will be seen that from the age of 20 onwards the frequency is about 2.5 pro mille. That the figures are dissimilar in the different years is probably due to random variation. These figures agree with our figures for 20–25 year-olds in Stockholm. It is to be expected that, when it is a matter of doing military service

Table 1. Number of diabetics per 1000 conscripts at the medical examinations in 1942–46.

Year	%₀₀ diabetics at the examinations
1942	2.41
1943	2.24
1944	2.59
1945	2.24
1946	2.48
1942–46	2.39

to prepare for the defence of their country, men are so keen on being exempted that they scrupulously report all disorders. Consequently, the official figures seem to be fairly correct, especially as all conscripts are subjected to a medical examination. In fact the irregularity apparently exhibited by the figures for men of 20–25 years is probably due to the increased number of known diabetics in the 20–21 year age group that depend on the drafting to military service. For women there is no corresponding irregularity.

As regards Switzerland I have been unable to find any corresponding age distribution of diabetics who have been given extra allowances of rationed foods. *Fleisch* (1947 a and b) has, however, statistically analysed the figures for the separate cantons from the point of view of correlation.

We shall briefly comment on *Fleisch*'s work. *Fleisch* has shown that the correlation is very close between the frequency of diabetics in the various cantons, on the one hand, and, respectively, income

tax, prosperity and the sum of life insurance premiums on the other. These coefficients of correlation lie close to 0.9 and are thus far higher than those usually found with respect to biological phenomena, as *Fleisch* himself emphasizes. Unfortunately, *Fleisch* published no primary figures and it is therefore impossible to check his computations. Probably, however, they are correct because *Fleisch* himself thought the close correlations were somewhat suspect and therefore he has probably checked them very carefully. Anyway, he feels justified in stating:

1. that the frequency of diabetes increases with mounting prosperity,
2. that the greater the number of intellectual workers there are in a canton the greater will be the number of diabetics,
3. that the greater the number of agriculturists, the smaller is the number of diabetics,
4. that the greater the number of extra allowances for other diseases the higher will be the frequency of diabetics.

On the basis of the last statement the author discusses to what extent the correlations may be due to the fact that the rural population does not apply for extra allowances for diabetes so often. To find out he calculates partial correlations and considers himself safe in assuming that the lastmentioned circumstance makes no great difference. Consequently he thinks that he actually has found a correlation between diabetes and standard of living. There is reason, however, to be critical of this last conclusion. Let us first consider the correlation with the insurance premiums. Obviously, when the sum of the insurance premiums increases, this on the whole implies that the number of people who wish to be insured is mounting. Life insurance companies generally have the condition of their clients medically examined (at least when the compensation is at all large), and this naturally uncovers some cases of diabetes. In such cases insurance is declined or granted against raised premiums. In any case it is obvious that the number of diabetics must increase when the sum of the insurance premiums increases because the disease will then become known more often. It may also be assumed that a population with a high standard of living can better afford insurance than others. Consequently it is evident that a correlation between the sum of life insurance premiums and diabetes at least in part must be due to the medical examinations. With regard to the correlation

between income taxes and diabetes it must be remembered that the data are fairly unreliable. The income tax is an indirect measure of prosperity but it is also conditioned by the honesty of the population concerned and by the frequency of fraudulent income tax returns. It is absurd to assume that there is a direct correlation between high income and diabetes as *Fleisch* emphasizes. In itself the income cannot in any way be the reason for any disease. It is equally faulty to assume that there is a correlation between the frequency of diabetes and the honesty of the population. The reason for the correlation must be looked for elsewhere. It may be taken for granted, though, that people in comfortable circumstances to a greater extent consult physicians and have access to physicians and that this in some measure must cause a correlation between high incomes and diabetes figures.

Another factor which also must be taken into account is that diabetes is decidedly more common in the higher age groups. (Cf. fig. 1.) Persons who have attained higher incomes and greater prosperity are naturally not very often young. It is usually only when one grows older that one is put in the higher income brackets or inherits fortunes.

Finally it must be emphasized that the correlation discussed does not apply to individual cases but to administrative units. If we now assume that the real frequency of diabetics is fairly constant in these units but that the registration varies with the average economic level, the result must be a very high correlation. As a matter of fact the high correlation coefficient obtained could hardly have any other explanation.

In summing up it may be stated that the figures given by *Fleisch* are not sufficiently conclusive for any positive statements to be made on their basis.

The Mortality in Diabetes.

Since, as we have mentioned, no direct data have been available one has attempted to use the mortality in diabetes in order to obtain a measure of the frequency of that disease. One does not seem to have discussed, however, how far one may go in using this method. In any case, this problem will here be discussed at rather greater length than is usual.

Provided that every one who becomes ill with a given disease also dies in that disease, the mortality may be used as a measure of the frequency of the given disease. If the person in question keeps

on living for a longer or shorter time after having contracted the disease, the mortality will naturally lag behind for a period corresponding to the mean duration of the illness. From these points of view the death-rate in cancer may be taken as an approximate expression for the frequency of cancer at onset.

The number of patients who recover after treatment is far too small to be of any statistical significance, provided that an approximation of the frequency of cancer is all that is required. If the figures have to be more exact one must attempt to correct for the small number of patients who recover after treatment, In practice, however, it is hardly possible to correct for this circumstance.

In diabetes, conditions are quite different. First and foremost the interval between onset and death is fairly long. Therefore many die of other completely irrelevant diseases or accidents. Many other deaths, again, are caused by disorders that are somehow related to diabetes, e. g. pneumonia. However, the correlation between diabetes and such diseases is not absolute. In the individual case it is extremely difficult if not impossible to tell whether the pneumonia was a consequence of the diabetes or whether it would have occurred independently.

Physicians, however, are prone to give diabetes as the reason for death even in such doubtful cases. The result is that the recorded death rate for diabetes includes cases of death from other causes, although it by no means includes all deaths among persons who suffer from diabetes. An illustrative example of this is that when the mortality goes down, e. g. owing to insulin treatment, the reduction will not be permanent. After some time the death rate again increases. The insulin treatment causes diabetics to live longer, but when the process has stabilized itself it does not reduce the number who are said to die from diabetes. (Insulin treatment more likely has the opposite effect, raising the death rate because more diabetics consult their physician in the knowledge that he can be of positive help. Hereby more cases of diabetes will in turn become known to doctors.) In fact the number of diabetic cases to an overwhelming degree depends on the extent to which physicians are aware of the occurrence of the disease. Deaths in diabetes will consequently be much more common among prosperous persons because they more often know the importance of treatment and of consulting a physician. When in time they die, the physician will in a comparatively large number of cases give diabetes as the main cause of death. With regard to poor

persons, who do not consult doctors so often for such vague symptoms, the physician will not as frequently be able to give diabetes as the cause of death. Under such circumstances the death-rate in diabetes may be expected to mount when the standard of living becomes raised and, for the same reason, the death-rate in diabetes will be higher in the better situated classes of society.

The most well-known analysis of the question of mortality and diet in diabetes has been given by *Himsworth*. Therefore we shall discuss his paper of 1935. To begin with he states the fact that in many countries the death rate of diabetes has risen steadily up to the present. He believes that this is because present-day diets are more rich in fats than diets of earlier days. The first thing that should be considered, however, is that the increase may be due to a more complete registration of the diabetic death rate or to some other irrelevant factor. It is a fact that official vital statistics have improved up to the present time. Moreover, our possibilities of discovering diabetes have increased not inconsiderably, especially as the number of physicians has become greater. The most important factor, however, is that longevity, particularly of diabetics, has increased and that partly for this reason the age composition of the population has altered. Obviously these changes must have very great effects. As appears from the previously given curve for diabetics in Sweden, the number of diabetic patients is much larger in the higher age groups. A displacement towards higher ages in the age composition of the population must therefore entail a greater mortality in diabetes, as must the smaller number of children. A displacement of this kind might in itself be enough to explain the raised diabetic death rate. *Himsworth* does not deal with these aspects of the question; he merely points out that a higher proficiency of the physicians cannot explain the differences.

The lowered mortality in diabetes at the end of the first World War to some extent suggests that a scanty diet is good for diabetics. The lowered death rate can, however, hardly be due to a lower frequency of onsets of diabetes when the diet is scanty. Then the effect would manifest itself much later. A reduced risk of contracting diabetes does not show up in the vital statistics until about a decade or so later.

When *Himsworth* goes on to discuss the difference in mortality between town and country populations, he finds for England and Wales that the rural population has a higher mortality. In the

United States the opposite is the case. Only in this connection does he discuss the importance of the age distribution, emphasizing that the figures for England and Wales and for the United States are not directly comparable. The differences due to age must first be corrected for. If this is done the differences vanish. When he then procedes to analyse the mortality in diabetes in different groups of society he omits to apply this view and refrains from correcting the figures for age differences.

In summing up it is probably safe to say that nothing can be proved with the aid of the figures in official vital statistics unless age differences are taken into account. Even then, it is impossible to draw any conclusions from the differences, because of the already mentioned circumstance that the frequency of known cases of diabetes influences the mortality figures to an extent which is very difficult to assess.

Several authors exist, both older and recent, who have advanced views like those of *Himsworth*. All of them are susceptible to criticism that in principle is similar to that given here. To our knowledge the only exception is *Schmidt* and *Sauermann* (1944). By means of special studies the authors show that the differences between various groups of society are mainly due to differences in age. The approximately 50 per cent lower mortality of the labouring population is wholly attributable to this. However, the authors attempt to calculate the risk of getting diabetes by means of very approximate methods. The resulting figures are so unreliable that they scarcely can be accorded any value, partly because the authors have been unable to take into account age differences for the risk of getting diabetes and base their exposition on the assumption that the risk of contracting the disease varies rectilinearly with the age. This is probably not the case.

Diabetes and Race.

In this connection it should be noted that the generally made statement, that jews especially often suffer from diabetes, must be considered absolutely unfounded. The statement is based on inconclusive vital statistics. Moreover, it has been found that the high mortality figures vanish if due regard is paid to the distribution of the material on various social classes. The high figures for jews are simply dependent on the fact that the analysed materials chiefly have come from groups of society in comfortable circumstances. The same, although in reverse direction, applies to negroes. Formerly it

was held that diabetes did not occur among negroes. It has later been found that this is fallacious. Probably there would be no difference in comparison with a white material of the same social status.

Experimental Diabetes Research and Diet.

There is much evidence suggesting that a diet poor in carbohydrates and rich in fats is favourable in diabetes. The blood sugar goes down and the symptoms more or less disappear. Animal experiments have yielded similar results. However, these studies are not very informative as to the problem of interest to us here, viz. if fats in the long run have a deleterious effect. The immediate effect may be favourable even if in the long run such diets are unfavourable.

Investigations made with the object of finding out the long-term action of fatty diets, however, are few and to some extent conflicting. The effect of fat in alloxan diabetes has been studied by *Burns*, *Kelsey* and *Lewis* and by *Abelin*. Despite different experimental conditions and choice of diet, both investigations lead to the conclusion that an increased supply of fats has a good effect, provided that such fats are used which are tolerated by the alimentary canal. *Janes* and *Prosser* arrived at the same result, whereas *Houssay* and *Martinez* drew a somewhat different conclusion. The latter authors experimented with rats from which most of the pancreas had been removed. It turned out that all those which had been put on a diet consisting mostly of fats died within 2 months. Of those given mostly carbohydrates 78 per cent died in the same period and of those given mostly proteins 56 per cent. This result has been interpreted to mean that fats are particularly dangerous and prevent recovery. However, this interpretation is not the only conceivable one. The figures may also indicate that those given much fats got little proteins and that the absence of some kind of proteins is the dangerous factor. The death rates, in fact, run parallel with the supply of proteins and not with the supply of fats. Besides, one has found that glutathion promotes recovery. The elements making up this compound are not present in fat but they may occur in protein. Perhaps this is why proteins are so necessary in the diet. In this connection is should be noted that *Wissler*, *Flindley* and *Frazier* (1949) have used forced feeding with glucose on a small number of rats. When the rats after somewhat more than one month were "sacrificed" they exhibited a fairly marked hyperplasia of the islets of Langerhans. This result is not unexpected. The marked hyper-

glycemia had probably necessitated a fairly plentiful production of insulin and therefore indirectly caused the hypertrophia. It should be mentioned, moreover, that these rats became excessively fat, probably because of the high blood sugar content.

Theoretical Aspects on Obesity and Diabetes.

We have shown that there is no support for the view that administration of fat should be harmful and that fat persons on account of their diet should run greater risks of getting diabetes than other people. Most likely cause and effect are related as follows. If the lack of insulin comes quickly, this causes sugar losses in the urine which lead to wasting. In young persons it is usual that the insulin deficiency sets in rapidly and is pronounced, whatever its cause may be. On the other hand, if the insulin deficiency develops slowly there will be a more prolonged intermediary stage when the blood sugar level is as high as is allowed by the renal barrier for sugar excretion through the urine. The reason for the increased appetite is the need for maintaining the blood sugar on a high level and this therefore causes increased deposition in the sugar depots. In this stage the patient will grow fatter because of the increased appetite. That fat persons "comparatively often contract diabetes" is therefore due to the fact that obesity may be a symptom of slowly developing diabetes. Besides, this form of diabetes occurs mainly in older persons. Probably, therefore, the situation is not that initially fat persons are susceptible to diabetes, but rather that persons who are susceptible to diabetes first grow fat before the symptoms become more serious and they begin to excrete sugar with the urine and become lean.

Summary.

1. The available figures concerning the frequency of diabetes and mortality in diabetes do not permit any conclusions as to whether increased administration of fats causes diabetes.

2. The few experimental investigations also do not permit any such conclusions.

3. From theoretical points of view it can most likely be expected that patients who contract diabetes slowly during an earlier period grow fatter and then develop symptoms of diabetes. With this in mind, we may suspect that adult persons who, without changing their habits in any way, begin to grow fatter later on will develop symptoms of diabetes.

Résumé.

1. Les chiffres disponibles concernant la fréquence du diabète et la mortalité dans cette affection ne permettent de tirer aucune conclusion concernant la relation de causalité entre une administration augmentée de graisses et le diabète.

2. Les quelques recherches expérimentales existantes ne permettent pas non plus de tirer de conclusions.

3. Au point de vue théorique, on s'attendrait plus probablement à ce que les patients qui sont atteints de diabète augmentent lentement de poids pendant une première période, puis développent la symptomatologie de l'affection. On peut donc soupçonner toute personne adulte qui prend poids sans changer ses habitudes d'aucune façon de développer plus tard un diabète.

Zusammenfassung.

1. Die Ziffern, über welche man betreffs Ausbreitung und Mortalität der Diabetes verfügt, lassen keine Schlußfolgerungen zu, daß vermehrte Fettkost Zuckerkrankheit hervorriefe.

2. Die geringe Anzahl experimenteller Untersuchungen lassen auch nicht irgendwelche derartige Schlußfolgerungen zu.

3. Vom theoretischen Gesichtspunkt aus liegt es am nächsten zu erwarten, daß Personen, welche Diabetes langsam bekommen, während der ersten Periode langsam fettsüchtig werden und erst dann Symptome von Diabetes bekommen. Von diesem Gesichtspunkt aus kann man den Verdacht haben, daß ein Teil der Personen, welche ohne Veränderung der Lebensweise im erwachsenen Alter ihr Gewicht zu vermehren beginnen, später Symptome der Zuckerkrankheit bekommen würden.

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THE NORMAL SIZE OF SELLA TURCICA

by BO NILSSON

In the system of endocrine organs that in part regulate the growth and functions of the body, the pituitary gland takes a central position. One might almost say that the pituitary gland is the brain of the endocrine organs. It is therefore natural to take an interest in the size of the pituitary gland in living man.

Initially investigators remained content with measuring the length and height of the sella turcica on X-ray photographs. This method was used in several investigations, for example those by *Gordon* and *Bell* (1922), *Royster* and *Rodman* (1922), *Enfield* (1922), *Le Coulm* (1923) and *Camp* (1926).

Obviously, however, this method yields a very unreliable and rough idea of the size of the sella turcica and consequently of the pituitary body. As early as 1925 *Haas* pointed out that it would be better to measure the area of the laterally projected sella than diameters of this area only. In order to determine the area, *Haas* traced on graph paper the sella on the radiograph and then he counted the number of squares within this outline. Using this method, one of his coworkers, *Kovacs* (1934), tried to arrive at normal values and variability for the size of sella turcica. His statistics, however, was unsatisfactory if not to say incorrect. Haas' method has been used, furthermore, by a number of authors, among whom the following may be mentioned: *Steiert* (1928), *Sartorius* (1929), *Wieser* (1933), *Klöppner* (1939) and *Mossberg* (1948).

In 1928, *Karlin* introduced the method of measuring the surface with a planimeter. Subsequently it has been discussed which outline of sella turcica should be measured. *Haas* (1925) maintained that two outlines were a sign of pathologic changes and indicated asymmetric excavation. Later, however, he abandoned this opinion. *Bokelman* (1932) tried to demonstrate that the area of the sella ought to be measured on the basis of the outline corresponding to the median plane. His reason for this view was that he had obtained good

agreement between the area in the median plane and a lump of modelling wax pressed into the sella turcica.

Furthermore, it would be interesting to know the strength of the correlation, if any, between the size of the sella turcica and the size of the pituitary gland, and it is unfortunate that this problem has not been sufficiently studied. *Bokelman* studied the largest number of cases, viz. 99, but he did not calculate any correlations and showed only that there is a relationship between small, medium and large areas of sella turcica and the size of the pituitary gland.

Ottaviani (1938) studied sella turcica in 61 persons (children and adults). His diagram and figures do not in any case suggest a strong correlation. Nor did he carry out any exact computations of the correlation.

The only investigator who has calculated any correlations is *Mossberg* (1948), who measured 27 cases. He found a coefficient of correlation of 0.92 between the logarithm for the volume of the pituitary body and the area of the sella. His standard error, however, is faulty, since it was computed from the conventional formula which does not hold for correlations as strong as in the present case. Moreover, it is also obvious that his number of cases is too small to yield reliable results, a fact that he himself calls attention to. This unreliability of *Mossberg*'s results may be elucidated by a comparison with *Ottaviani*'s figures. These cannot possibly yield a coefficient of correlation of the magnitude stated by *Mossberg*. In other words, the problem must, by and large, be considered unsolved. Further investigations are in any case required if the size of the correlations is to be determined. However, some correlation obviously exists.

The investigations mentioned above give the means for different ages. It is remarkable, though, that the standard deviations around these means have been disregarded. In this respect the only exception is *Mossberg*, who has calculated the standard deviation for various age groups. However, his cases were far too few to permit a reliable conception of the magnitude of the standard deviation.

Obviously, even without exact normal values it is possible to sort out sellae corresponding to highly pathologic pituitary bodies on the basis of general knowledge. It is, however, equally obvious that if more exact normal values were available, i.e. means and variability, it would be easier safely to distinguish between normal and pathologic pituitary glands. By the way, one may in any case expect to find a correlation between the sella turcica and the pituitary body

when the material includes pathologic cases. What the case is when the material comprises solely normal individuals is, as is pointed out above, still not quite clear.

In this paper an attempt will be made to define the variability in normal male adults, i.e. men of 21 years, and also to give some idea of the corresponding variability in boys of 12 years.

The material for the present study is composed of radiographs which were taken by Doctor *Arne Björk* for his investigation concerning prognathism. I sincerely thank him for putting at my disposal his material. I also wish to thank Professor *Gunnar Dahlberg* for suggesting this investigation and for his advice and help. The reader is referred to *Björk* (1947) for full particulars of the material. Here it will suffice to mention that it comprises conscripts of 21 years of age, and because of that to some extent they may be regarded as selected. Persons exhibiting signs of disablement or disease are supposedly not included among cases of this type. However, this selective factor would seem to be without importance, since the object of the study is to find out how things are in healthy persons. The material also includes boys of 12. In Västerås all but 6 school children of this age have been X-rayed. This part of the material may also be regarded as fully representative.

It will be seen in *Björk*'s publication that the photographs were not taken under the best conditions. Owing to the method adopted, sella turcica became partly obliterated by various pieces of apparatus. Quite a number of the pictures were therefore useless for the present purpose. The remaining material comprises 210 persons of 21 years and 239 boys of 12.

As regards the photographing *technique*, it will suffice to say that the pictures were taken in lateral projection and oversized by about 6 per cent in length and breadth, i.e. about 12 per cent in surface area. This error is corrected in the calculations. The measurement of the sella turcica on the photographs was carried out as follows. The external and internal delimitation of the sella outline was filled in directly on the radiograph with an Indian ink pen for fine lines. In solitary cases the delimitation of the sella was sharp, but more often it was broad, corresponding to the difference between the medial and lateral prophiles. The two areas were then measured with a planimeter. The selected upper border was a line between the lowest point on the outline of Tuberculum sellae and the innermost point on the tip of the dorsum.

The standard error of measurement was determined by means of 25 duplicate determinations with the outline being redrawn between the two measurements. In so doing the outlines were not inked in, since the pen would scratch the photograph so that guiding marks might remain even after the first lot of ink had been washed away. Instead a soft and sharp pencil was used and its marks could be removed without leaving the slightest trace. The standard error of measurement was calculated according to the formula $\sigma_i = \pm \sqrt{\dfrac{\Sigma d^2}{2n}}$,

in which d is equal to the difference between the two related sets of measurements and n = the number of cases (cf. *Dahlberg*, 1940). σ_i was determined to ± 2.6. This is 4.2 per cent of the mean. This error of measurement includes only errors of observation and not photographing errors. However, as the photographing process was conducted under standardized conditions, the latter error should be negligible.

It is known that the skull is fully developed far earlier than the rest of the skeleton. According to *Martin* the skull grows most during the first years of childhood. The growth taking place after the 10th year of life is very moderate and gradually becomes negligible. It has been impossible to give an exact time when the skull may be considered fully developed. It appears from *Björk*'s paper that from 12 to 21 years of age there is a slight growth. The anterior part of the base of the skull between the nasion and the centre of sella turcica increases by 4.5 mm, i.e. 6.5 per cent. In comparison it may be mentioned that Ramus mandibulae increases by 11.1 mm, which corresponds to 26.3 per cent. This illustrates that from 12 to 21 years of age the facial skeleton grows far more than the skull, but naturally the growth of the facial skeleton is also far greater before the age of 12.

On examining the photographs it turned out that the difference between the exterior and the internal outline amounted to approximately 9 sq. mm. In the computations the mean of the values for the two outlines will be used. The result appears in table 1, where the observed values are given. It will be noted that there is an insignificant excess and a small skewness for both 12 year olds and 21 year olds. For the latter the mean was 65 sq. mm with a σ of 15 sq. mm, implying that the greatest value (calculated on a variability of 6) is 110 sq. mm and the smallest 20 sq. mm. The greatest value for 12 year olds will be 87 sq. mm and the smallest 27 sq. mm, the mean being

Table 1.

Mean and standard deviation in square millimetres of the size of Sella Turcica, as well as Skewness and Excess, calculated on the basis of the means of the medial and lateral prophiles in 239 boys of 12 and 210 men of 21. The observed values of the enlarged radiograms are reduced to real values.

	Boys of 12	Men of 21
Mean ± standard error	50.98 ± 0.61	58.41 ± 0.94
Standard deviation ± standard error	9.35 ± 0.43	13.55 ± 0.66
Skewness ± standard error	−0.163 ± 0.071	−0.413 ± 0.076
Excess ± standard error	0.077 ± 0.036	0.175 ± 0.038

57 sq. mm and the corresponding standard deviation 10 sq. mm. It will be noted from these figures that the distribution is rather flat. The deviations from the normal curve are probably due to a few extreme values and are of no major importance. Of course, it is not impossible that a few individuals with a pathologically enlarged pituitary gland have been included among the examined cases, since they had not so far exhibited signs of hypophysial disorders. The distribution of the sellae turcica of the 21 year olds appears in fig. 1.
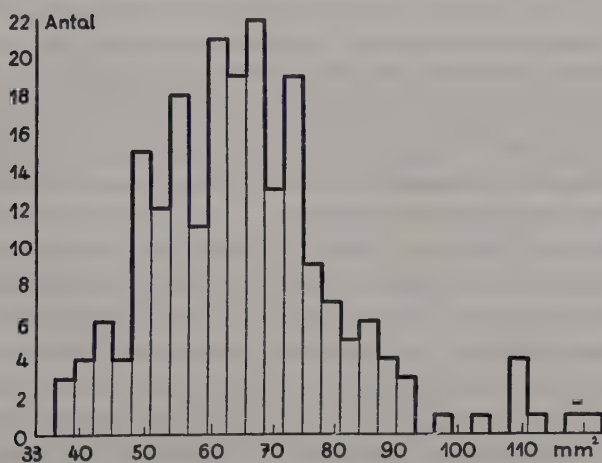
Fig. 1. Distribution of the size of sella turcica. The largest value found and the corresponding expected value is 120, respectively 110 sq. mm. The smallest value found and the corresponding expected value is 6, respectively 20 sq. mm. The discrepancy between these figures is due to the skewness of the distribution.

Summary.

Figures for the size of sella turcica on radiographs of normal men of 12 and 21 years of age are given. It is shown that the range of variation is rather large (see table 1) and that the distribution is slightly skew.

Résumé.

L'auteur donne des chiffres concernant la dimension de la selle turcique sur les radiographies d'hommes normaux entre 12 et 21 ans. Il montre que l'échelle de variation est assez large (table 1) et que la distribution est légèrement oblique.

Zusammenfassung.

Die Ziffern werden hinsichtlich der auf Röntgenfotos festgestellten Größe der sella Turcica bei normalen männlichen Individuen im Alter von 12 resp. 21 Jahren gegeben. Es zeigt sich, daß die Variationsbreite ziemlich groß ist (siehe Tabelle 1) und daß die Verteilung etwas schief ist.

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THE DISTRIBUTION OF STATURE
IS HYPERNORMAL

by CORRADO GINI

The conviction that physical and biological phenomena are distributed normally in conformity with the Gaussian curve—known as "normal" just for that reason—has been and still is so wide-spread that this supposition is used as the basis not only for forecasting the departures from a distribution of which only the average and the standard deviation are known, but also for measuring the variability and correlation of quantitative phenomena classified in qualitative categories, as well as in the theory of samples. Generally speaking, wherever there is no reason for believing otherwise, the supposition is that the distribution is normal, and the bearing of the fact that this supposition does not correspond to the truth is not always enquired into.

This conviction dates back to *Quetelet* who, having found an approximate correspondence between the distribution of stature and the thoracic perimeter (chest measurement), as also of temperatures, with binomial distribution, had no hesitation in declaring that the said law is not only applicable to stature but holds good also for the measurements taken of the different parts of the body, and indeed of all living beings, whether animal or vegetable, and is also found in a very marked degree in physical phenomena, more especially in those of meteorology[1]).

Moreover, many enquirers have been confirmed in this conviction by the examination of the distributions of the various measurements taken of men and other living beings, when finding that they conformed to more or less strictly symmetrical curves of campanular form. As a matter of fact, however, only rarely has an accurate comparison been made between the data observed and those theoretically corresponding to the normal curve, and when this comparison has been made and notable divergencies have been met with, and still more so when without any comparison they were strikingly obvious, there has

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[1]) *Anthropométrie ou mesure des différentes facultés de l'homme.* Brussels, Muquardt, 1871, p. 292.

been a tendency to neglect making a strict examination, and to ascribe the said divergencies to the effect of random variation due to the limited number of observations (so giving to the data observed the value of a sample) or to ascribe them to the effect of a selection. It was thought that had the whole mass of cases been observed it would have been found that the correspondence was satisfactory, just as in the case of *Quetelet*'s enquiries.

Indeed, as a result of the examination of the distribution of chest measurements and statures obtained for the conscripts or soldiers in Belgium, France, Italy and the United States of America, *Quetelet* believed that he was justified in concluding that the correspondence was quite satisfactory[1]). After him this conclusion was accepted without opposition and was reconfirmed by those who discussed the matter. In the case of stature in particular *Quetelet* had not failed to take into consideration the difference found in the Belgian statistics[2]) between the observed and theoretical distributions, accounting for them by explanations which to him and to the others who dealt with the matter after him, seemed plausible, so that, while many admit, in opposition to *Quetelet*'s hasty generalisation, that the distribution of many biological and physical phenomena is not normal, the distribution of stature has been and is currently held to be a typical example of the normal curve.

When several years ago, before the second world war, I had the students of the Faculty of Statistical Demographic and Actuarial Sciences of the Rome University make studies on the distribution of the statures of the conscripts[3]), I was therefore much surprised at finding that the curves of stature in Italy were definitely hypernormal both for Italy as a whole and for the separate regions. The enquiries were then interrupted but have since been taken up again for Italy and extended to other countries, thus allowing of conclusions which, at least in the case of the populations studied, may be considered reliable.

A distribution can be described as *hyper-normal*, or *hyper-binomial* or *excessive* or *leptokurtic* when, on comparison with the

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[1]) *Anthropométrie*, op. cit. p. 286–287. – *Physique sociale ou Essai sur le développement des facultés de l'homme*. Brussels, Muquardt, 1869, Vol. II, Bk. III, Ch. 1, No 2: *Loi de distribution des tailles quand le nombre des chances est illimité*, pp. 38–76.

[2]) *Physique sociale*, op. cit. pp. 61–71.

[3]) Attention should be drawn to the fact that here and in the following of this article the word "conscript" means all the men entered on the list of levies and not only those fit for military service.

normal, it offers a greater frequency of central values and of terminal values, and consequently a lesser frequency of values inter-mediate between the former and the latter ones.

Italian army statistics supply material particularly well-suited for such enquiries as since 1854 and until the end of 1920 they contain data on the distribution of stature, classified in centimeters, for all the men called up for the army, and not only for the country as a whole but (except in 1917) also for the separate regions and in each region for the separate provinces or districts (*circondari*); over a period of some years both for the former and for the latter[1]). They are classified in two tables, one for all the men entered on the lists of levies for the year, inclusive of those remanded from previous levies who are again examined; the other for those entered on the list of a given year, born in the year corresponding to it. It would be preferable to make use of this second table as duplications are thus avoided; but during a first period (that until 1873 inclusive) only the first table was published while in the later years (from 1911 onwards) only the second one was printed. The comparisons made for some years for which both tables are available, have shown nevertheless that, as far as hypernormality is concerned, the difference in the results is negligeable, so, for the purposes of this paper, it has been possible to hold as equivalent the distributions of the two tables, using the second when available and only in its absence making use of the first.

As our measure of hypernormality we have taken the ratio between the double variance and the square of the mean deviation from the arithmetical mean whose theoretical value, supposing the distribution is normal, is: $\pi = 3.1416$[2]). It is to it we refer in this paper when speaking of the index of hypernormality.

The following table (Table 1) gives the actual values of the index for the conscripts born in the years 1854, '70, '80, '90, 1900, 1915, and 1920, both for the Italian regions and for the national territory as a whole. As can be seen, the 116 values found steadily exceed the theoretical value 3.1416 except in the case of Latium in 1920[3]).

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[1]) Ministero della Guerra. *Delle leve di terra sui giovani nati nell'anno. . .* Roma.

[2]) This index has been used because its construction lends itself to a ready control of the operations, and it is therefore particularly well suited to work entrusted to students. For a discussion of the several indices of hypernormality, see our article *Asimmetria e anormalità delle serie statistiche*, now in the press, "Metron" Vol. XVI.

[3]) The calculations were made in the Institute of Statistics of the Rome University under the direction of the Assistant, Dr. *Giacomo Sonnino*.

Table 1. Indices of hypernormality for Italy and Italian Regions.

Regions	Years of Birth						
	1854	1870	1880	1890	1900	1915	1920
Piedmont	3,484	3,353	3,335	3,321	3,375	3,232	3,258
Liguria	3,321	3,254	3,363	3,271	3,275	3,301	3,274
Lombardy	3,457	3,410	3,298	3,328	3,326	3,268	3,247
Venetia	3,295	3,297	3,238	3,332	3,354	3,228	3,270
Emilia	3,263	3,262	3,295	3,283	3,331	3,260	3,228
Tuscany	3,249	3,261	3,218	3,146	3,304	3,193	3,240
The Marches	3,280	3,228	3,230	3,236	3,344	3,251	3,261
Umbria	3,264	3,239	3,275	3,452	3,359	3,302	3,226
Latium	3,312	3,446	3,429	3,346	3,351	3,292	3,064
Abruzzi and Molise . . .	3,257	3,363	3,347	3,238	3,264	3,161	3,206
Campania	3,300	3,355	3,294	3,294	3,276	3,198	3,330
Apulia	3,483	3,370	3,472	3,301	3,316	3,318	3,198
Basilicata	3,367	3,530	3,376	3,280	3,292	3,305	3,382
Calabria	3,429	3,562	3,368	3,354	3,294	3,216	3,182
Sicily	3,336	3,390	3,357	3,430	3,386	3,254	3,295
Sardinia	3,396	3,408	3,333	3,466	3,434	3,196	3,301
Tridentine Venetia . . .	—	—	—	—	—	3,245	3,433
Julian Venetia and Zara .	—	—	—	—	—	3,274	3,189
Italy	3,350	3,344	3,320	3,288	3,339	3,224	3,231
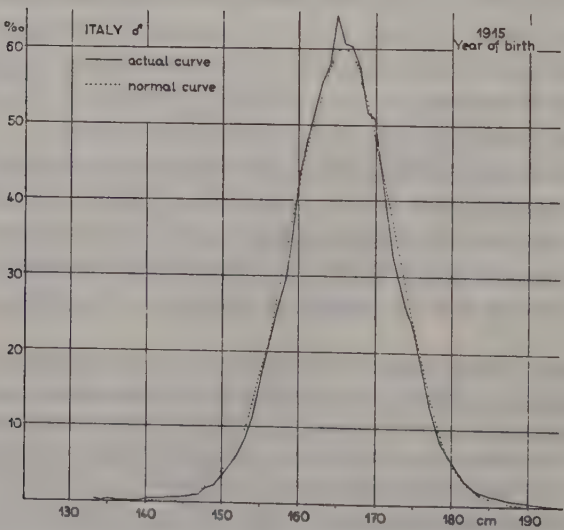
Fig. 1.

Table 2. Distribution of 120 indices of hypernormality for the Italian Regions.

Values	Frequency
< 3,1416	1
3,1416 – 3,15	1
3,15 – 3,17	1
3,17 – 3,19	2
3,19 – 3,21	5
3,21 – 3,23	11
3,23 – 3,25	11
3,25 – 3,27	14
3,27 – 3,29	12
3,29 – 3,31	13
3,31 – 3,33	10
3,33 – 3,35	9
3,35 – 3,37	8
3,37 – 3,39	5
3,39 – 3,41	3
3,41 – 3,43	5
3,43 – 3,45	2
> 3,45	7
Average	3,31

Table 2 shows the distribution of the values found for the separate regions[1]). The maximum frequency is found in the classes from 3,22 to 3.33, with a mean of 3.31.

Similar calculations were made for the separate provinces of Tuscany and Lombardy for the conscripts born in the year 1915 (Table 3) and here again the values found were constantly superior to the theoretical value, except for the province of Leghorn.

The summaries of the statistics of the levies published in France[2]) contain tables similar to those for Italy. Only in the case of the conscripts born between 1903 and 1922 (the data for 1913 and 1915 are missing) is however the classification made with sufficient detail to

[1]) The values classified in Table II are 120; besides the 116 values of the separate regions entered in Table I, they include the 4 following values: Marches, 1872: 3.226, Umbria, 1872: 3.300, Latium, 1905: 3.221, Abruzzi and Molise, 1905: 3.234.

[2]) *Compte Rendu sur le Recrutement de l'Armée pendant l'année* .... Paris, Imprimerie nationale.

Table 3. Indices of hypernormality for the Provinces of Lombardy
and Tuscany (1915).

| Lombardy | | Tuscany | |
Provinces	Indices	Provinces	Indices
Bergamo	3,262	Arezzo	3,226
Brescia	3,168	Florence	3,206
Como	3,234	Grosseto	3,186
Cremona	3,286	Leghorn	3,118
Mantua	3,235	Lucca	3,240
Milan	3,238	Massa Carrara	3,258
Pavia	3,245	Pisa	3,163
Sondrio	3,401	Pistoia	3,329
Varese	3,190	Siena	3,218
The whole Lombardy . .	3,268	The whole Tuscany . .	3,193

allow of a reliable determination of the index of hypernormality[1]).
In this case also the index is constantly superior to its theoretic value
(Table 4) varying from 3,20 to 3.32, with a mean of 3.24.

In *Winkler*'s treatise on statistics[2]), we find the distribution of
stature in the case of the conscripts of the rural district of Mistelbach
in Lower Austria for 1913 and here again the index shows hyper-
normality, being equal to 3.20.

Special importance attaches to the results of the anthropo-
metrical enquiry made in Switzerland, under the direction of Prof.
O. Schlaginhaufen, on the youths who, over a period of six years,
were called up for military service (each year the young men of one
of the 6 recruiting districts were examined[3]). These figures are parti-
cularly important as we can be certain that, gathered as they were
by an experienced anthropologist with the help of a specially trained
technical staff and with all modern measuring instruments, there can
be no doubt about the accuracy of the measurements and the reliabi-
lity of the results.

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[1]) I owe the communication of the figures to the courtesy of Prof. *Pierre
Delaporte.*

[2]) *Grundriß der Statistik. I. Theoretische Statistik*, zweite Auflage, Wien, Manz-
sche Verlag, 1947, p. 35.

[3]) *Anthropologia Helvetica I. Die Anthropologie der Eidgenossenschaft*, Zürich,
Füssli, 1946.

Table 4. Indices of hypernormality for France.

Years of birth	Indices
1903	3,212
1904	3,225
1905	3,215
1906	3,201
1907	3,222
1908	3,246
1909	3,242
1910	3,245
1911	3,245
1912	3,226
1914	3,249
1916	3,261
1917	3,324
1918	3,285
1919	3,293
1920	3,317
1921	3,268
1922	3,217
The whole period	3,244
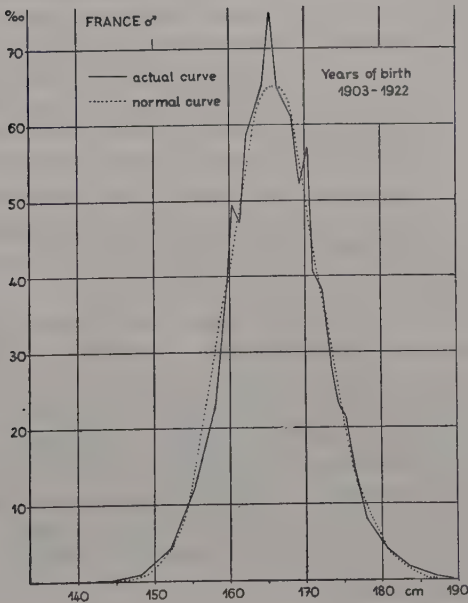
Fig. 2.

Here again the distribution is found to be hypernormal, the index value being = 3.28[1]).

The accuracy of the Swiss returns suffices for eliminating definitively the explanations, given by *Quetelet* himself, of the divergencies between the theoretical curve and the actual data as supplied by the Belgian statistics at his disposal. He had indeed remarked that the said statistics presented a much higher frequency of low statures than the theoretical one, and on the other hand a greater frequency in the central group. But he considered that these divergencies should be accounted for by inaccuracies in the returns. The first divergency was indeed assigned by him to the tendency of the conscripts to lower their stature artificially below the exemption limit [2]). For the second divergency he suggested several explanations which indeed it is difficult to reconcile to one another. In some passages it was ascribed to the desire of the conscripts to raise their stature in order to reach

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[1]) There are distributions of stature for other populations, but the information we possess on the modalities of the returns are insufficient to allow us to have full confidence in the indices obtained from them.

In the case of Turkey, returns covering 39,465 males and 20,663 females, from 20 years of age upwards, were obtained by a special enquiry made by specialised workers in 1937. The data were published in the Publication No. 15 of the Central Statistical Office of the Turkish Republic (*Enquête Anthropométrique, faite sur 59,728 individus des deux sexes*, Ankara) and in the thesis presented for her degree in Sociology by Miss Afet Uzmay to the University of Geneva (*Recherches sur les caractères anthropologiques des populations de la Turquie*, Université de Genève, Faculté des Sciences économiques et sociales, Imprimerie Albert Kündig, 1939). The index shows a slight hypernormality both for the males (3.180) and for the females (3.170); but the reports do not show the criteria by which the subjects were selected.

Other data of a very limited scale relating to the Lapps have been deduced from a paper by *S. Wahlund: Anthropometry of the Swedish Lapps* (in *G. Dahlberg* and *S. Wahlund, The Race Biology of the Swedish Lapps*. The Swedish State Institute of Human Genetics and Race Biology, Uppsala, 1941).

They refer to 581 males and 606 females from 15 years of age upwards. The distribution seems to be hypernormal for the males (3.274) and practically normal (3.130) for the females. It is quite likely that the normality of this latter distribution depends on the small number of the observations. Indeed, a comparison of the actual curve with the theoretical curve (see the diagrams) for the females as well as for the males, reveals a tendency for the central and terminal observed values to exceed the theoretical ones, which is characteristic of hypernormal distributions; but the irregularities dependent on the scanty number of observations are so marked that the value of the index is disturbed thereby.

[2]) *Physique sociale* etc., op. cit. 63.

the limits fixed for entry into their favourite regiments[1]). But this might have accounted for a larger number of conscripts classified in that group due to a transfer from the lower one, but not also due to a transfer from the higher group, as the figures seem to suggest. Some pages further on *Quetelet* himself had recourse to another explanation; he asserted that in the case of medium statures, they were not measured but judged by sight, so that many conscripts who were assigned to the group in question would have been placed either in a lower or in a higher group [2]), if accurate measurements had been taken.

Whether these supposed inaccuracies occurred or not in the Belgian returns for stature of which *Quetelet* made use, similar inaccuracies must certainly be excluded not only, in the case of the Swiss returns, for the reasons above stated, but also in the case of the Italian, French and Austrian returns for conscripts because the distributions deduced from them are symmetrical and do not show a higher frequency of low statures than of high ones, which should be the case if *Quetelet*'s supposition were correct, and which does indeed occur in the case of the distribution of the Belgian statures reproduced by *Quetelet*.
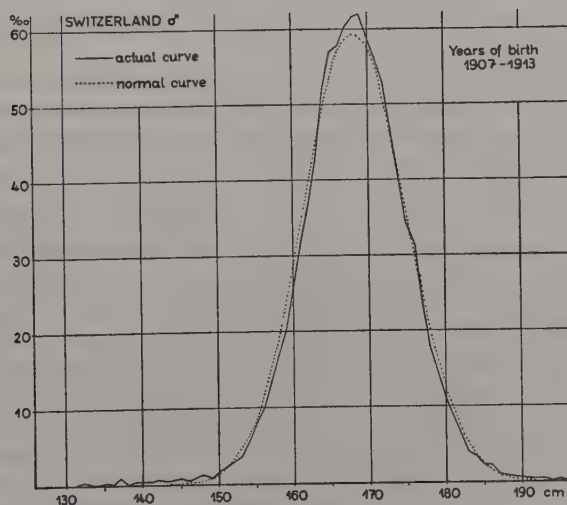
Fig. 3.

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[1]) Ibidem, pp. 63; 65.
[2]) Ibidem, p. 71.

The symmetrical distribution of the Italian and French statures is clearly shown by a graph in which the normal theoretical curves are superimposed on the curves of the actual data. It will be noted that the French curve, although referring to a very large number of cases (5,044,925), offers marked irregularities corresponding to the round figures which finish with 5 or with 0. Evidently the measurements of stature of the conscripts by the army doctors are less accurate in France than in Italy.

As the most frequent stature coincides with a round figure (165 cm), the curve corresponding to it forms a very sharp peak; but the impression of hypernormality given by the curve, as well as its measure given by the index, are not accentuated thereby, because also in the case of the contiguous values (164–166) the frequencies, though somewhat attenuated, nevertheless exceed the theoretical frequencies.

And here we may wonder why on earth *Quetelet*, and after him so many other statisticians, have considered the distribution of stature to be normal. The fact is that the distributions they were considering were incomplete. They generally referred to soldiers on service or to conscripts fit for military service, from whose numbers were excluded all the rejected conscripts, among whom were all those whose height was below a certain limit and many who were very tall. Thus the extremes were excluded [1]) Other series used by the statisticians

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[1]) Some very wide enquiries have been made about soldiers. One of them deals with the Italian soldiers born in the years 1859—63 and has been published by Dr. *Ridolfo Livi* in the *Antropometria militare* (Part II, *Dati demografici e biologici*, Roma, 1905). It concerns 299.355 individuals, of which 256.166 of 20 years of age. For their 256.166 statures, the index of abnormality is 3,09, i. e. somewhat inferior to its theoretical value. Two other important investigations refer to Swedish soldiers. The results of the first one, made in the years 1897 and 1898, have been published by *G. Retzius* and *C. M. Fürst* (*Anthropologia Suecica*, Stockholm, 1902). The distribution of stature concerning 44.939 individuals gives an index of abnormality of 3.16. The results of the second investigation, made in the years 1922-24, have been published by *H. Lundborg* and *F. J. Linders* (*the Racial Characters of the Swedish Nation.—Anthropologia Suecica MCMXXVI*, Uppsala 1926). As concerns stature, it refers to 47.387 military trained conscripts and regular soldiers, aged from 20 to 22 years. The editor of the present journal, Dr. *G. Dahlberg*, who measured most of the soldiers himself and controlled the measurements of the others, kindly writes to me that for the distribution of statures he obtains an index of abnormality of 3.12. Thus we may say that the two distributions of the Swedish soldiers are practically normal, while that of the Italian soldiers is somewhat hyponormal. This difference is not surprising, as the effect of selection for military service on stature is less pronounced for a taller population.

were obtained by anthropologists who measured the adults with whom they came into contact, and here again we may suppose they were less likely to measure abnormally proportioned persons partly because such persons are often diseased, partly because when healthy they are somewhat reluctant to go about in public. More-over, when the mean of a character increases or decreases with age, it is to be expected that the distribution of the individual measure-ments concerning adults of various ages be less hypernormal or more hyponormal than the corresponding distribution for adults of the same age[1]).

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Having ascertained the fact that the distribution of stature is, at least in the countries above considered, really and definitely hyper-normal, we must now enquire why.

Two hypotheses may be advanced: that it depends on hyper-normality of local distributions, or, these being normal, on hyper-normality of the distribution of the average statures in the separate localities. The average stature indeed differs, as is commonly observed, systematically from one locality to another, but if the distribution of the local averages is normal and the local distributions are also normal and have the same variability, then the total distribution covering the statures for all the localities will also be normal.

Now, the fact that the distribution of stature should be hyper-normal in so small a district as that of Mistelbach makes the first of these hypotheses unconvincing; and it must be excluded when we come to the comparison between the indices of hypernormality found in the distribution figures for the whole of Italy and the averages of the indices found for the separate regions. It must also be excluded on the basis of the comparison between the indices of hypernormality of Tuscany and of Lombardy and the averages of the indices found for the respective provinces. As can be seen from the following table (Table 5), the indices for the total populations are not superior, but indeed on the average inferior, of the averages of the indices for

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[1]) After this article had been written, indices of abnormality have been calculated for the distributions of many other characters besides stature for several populations. The distributions for conscripts of about the same age are gener-ally hypernormal, while those referring to data collected by the anthropologists for the adults of various ages are often nearly normal or hyponormal.

Table 5.

Years	Averages of the indices of hypernormality for the Regions	Index of hypernormality for Italy
1854	3,343	3,350
1870	3,358	3,344
1880	3,327	3,320
1890	3,317	3,288
1900	3,330	3,339
1915	3,250	3,224
1920	3,255	3,231
Averages	3,311	3,299

Regions	Averages of the indices of hypernormality for the Provinces	Index of hypernormality for the Region
Lombardy	3,251	3,268
Tuscany	3,216	3,193
Averages	3,234	3,231

sections of the populations[1]). We are therefore led to the conclusion that hypernormality occurs also in the case of the local distributions.

One might seek for another explanation in the hypothesis that the distribution of stature is the resultant of two curves, both normal, one wider and the other narrower. This, indeed, is the explanation *Ludwig* gave of the hypernormality of the curves that is frequently observed, more especially in the case of plants[2]) and in some cases it may be plausible. In our case also this hypothesis may, at first sight, seem acceptable, considering that two groups of factors concur in determining the characteristics of living beings and in particular the height of man: on the one hand, hereditary factors and on the other environmental.

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[1]) Indices of abnormality were also calculated for the averages of the regions of Italy and for those of the provinces of Tuscany and Lombardy. All of them turned out to be inferior to the theoretical value $\pi = 3.1410$.

[2]) Cfr. "Botan. Zentralblatt" 64 and 68, 1895–96. See on this subject *W. Johannsen, Elemente der exakten Erblichkeitslehre*, 1913, p. 254 et seq.

Quetelet supposed that as a result of heredity the statures of a population would have been all equal and that the differences from one person to another would depend on environmental factors[1]). The investigations of uniovular or biovular twins have shown that this is not so and that on the contrary the differences between the characters of different persons are to be ascribed for the most part to hereditary factors and in a minor degree to environmental ones. It might therefore be supposed that each of these two groups of factors is matched by a curve—wider for the hereditary and narrower for the environmental factors—and that the hypernormal curve is given by the sum of both of them.

But this explanation is not acceptable because, as a matter of fact, it is not environmental factors that act on one group of the population and hereditary factors on another, but both groups of factors act simultaneously in combination on all the persons.

It remains to be seen if an explanation can be found of the way in which the separate factors in the same group act on one another, or else of the way in which the factors of one group combine with those of another.

In the case of hereditary factors it is evident that a characteristic determined by a single factor, which is transmitted without dominance, in conformity with the Mendelian scheme, will give rise to a symmetrical hypernormal curve presenting one intermediate group corresponding to the heterozygotes and two terminal groups corresponding to the two groups of homozygotes.

It is true that the hypernormality may be attenuated—and theoretically even eliminated or else replaced by a hypo-normality—as a result of the phenomenon of transvariation between heterozygotes and homozygotes, due either to individual differences in the intensity of the hereditary factors, or to the difference of environment during the period of development.

On the other hand, if a characteristic depends on two factors that are inherited according to the Mendelian scheme, each of which allows of two allelomorphs one of which dominant over the other, but which are such that in one factor the allelomorph which tends to determine a low stature is dominant, and in the other the allelomorph that tends to determine high stature, then, apart from any trans-

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[1]) See on this matter *Anthropométrie*, op. cit. pp. 15 and 16, and *Lettres sur la théorie des probabilités*, Brussels, 1846, Letter XXX more especially on p. 216.

variation, their combination will give rise to a hypernormal symmetrical distribution. Here again, of course, the phenomenon of transvariation may attenuate or, theoretically, eliminate the hypernormality, even giving rise to a hypo-normality.

Experience however shows that there are well-grounded reasons for believing that stature depends on many factors, and the combinations of various factors may of course also determine a curve that differs substantially, even from the point of view of normality, from those curves to which the action of each of the component factors would give rise. But what the number of these multiple factors is, whether the partial or total dominance of an allelomorph occurs or not in each of them, whether the dominance does or does not occur in the same sense for the separate factors, whether the action of the separate factors is independent or concordant or on the contrary compensatory in character, and lastly, what may be the bearing of the transvariation, are all questions to which we are unable to give an answer. What we have said only let us glimpse the possibility, and nothing more, of finding an explanation of the hyper-normality of the distribution of stature.

As far as environmental factors are concerned, there are undoubtedly good reasons for believing that they do not give rise to a completely normal curve, for all the factors are not in a monotone relation to stature. There are, indeed, some factors that exercise a more favourable influence on stature when they act with intermediate intensity, while with a higher or lower intensity they act unfavourably. The notion of "*aurea mediocritas*" holds good, as is known, for the action on man of many environmental factors, such, for instance, as temperature, nutrition etc.

These considerations would lead us to expect that, due to environmental factors, the distribution would be asymmetrical with an index of negative dissymmetry. But the observed data show that we cannot affirm the existence of a marked positive or negative dissymmetry, neither for Italian nor for French statures[1]). In the distribu-

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[1]) This conclusion differs from that reached by S. *Alberti*, who in a detailed study on the *Influenza della eliminazione della mortalità sulla composizione qualitativa e sulla dinamica della popolazione*. (Roma-Sormani, 1939) has examined the asymmetry of the distribution of statures of the conscripts of 12 provinces of Italy in the period 1854-56 (inclusive of those remanded from previous levies) and in 1908 (inclusive and exclusive of those remanded from the previous levies). *Alberti* found negative indices of dissymmetry for all the 12 provinces in 1854–56 and for 8 or 11

tion of Swiss statures the diagram clearly shows a negative dissymmetry, but it is limited to the extreme end of the distribution, and should probably be ascribed not so much to the circumstance above mentioned, but rather to the presence in several Swiss valleys of cretinism which, as is known, is associated with very low stature. In any case, even supposing that this circumstance might explain asymmetry in the distribution of statures, one cannot see how it could explain hypernormality.

On the other hand, the curve might show a trend towards hypernormality as the result of a compensation occurring either between the action of the separate factors of the hereditary group, or between the action of the separate factors of the environmental group, or, lastly, between the action of the two groups of factors. One cannot well see how a compensation could occur among the separate hereditary or among the separate environmental factors. But it would seem admissible that a compensation should occur between the two groups of factors, in the sense that when the environmental conditions are more unfavourable, then selection is stricter, and therefore hereditary factors are favoured. This does not however necessarily mean that the result will be a hypernormal distribution. This result would indeed occur if the compensation were to take place between not very marked variations of the hereditary and of the environmental character so as to make the deviations of mean size less frequent, while the slight ones which would take their place would be more frequent. On the other hand, were the compensation to occur only between terminal deviations, hyponormality of the distribution might be the result because thereby the terminal deviations would be made less

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out of 12 provinces in 1908, the difference in the figures depending on the inclusion or not of those remanded from previous levies. But *Alberti* had adopted as index of asymmetry the third moment divided by the cube of the standard deviation, an index, which gives excessive importance to the terminal deviations. On the contrary, our conclusions are based on the index of dissymmetry—which seems more rational to us—based on the difference between the mean and the median, which is equal to the mean of the differences between the intensities of the symmetrical deviations (see the article *Asimmetria e anormalità delle serie statistiche* to be published in Volume XVI of "Metron" but to which reference was made as far back as 1941 in the Review: *Recenti contributi alla metodologia statistica*, "Vita Economica Italiana" 1st Quarter 1941, p. 38, by Dr. *E. Pizzetti*. See also *A. Costanzo: La statura degli italiani ventenni nati dal 1854 al 1920* in "Annali di Statistica" Series VIII, Vol. II, 1948, in which the indices of dissymmetry, based on the ratio of the third moment to the cube of the standard deviation, are calculated for Italy as a whole and for the separate regions of 1874 and 1918.

frequent, and those of average size to which the others would be re-
duced more frequent. This also is a problem to be studied as in any
case it opens the possibility of finding another explanation of the
hypernormality of the distribution of statures.

Summary.

It is shown that in quite a number of anthropometric inves-
tigations the distribution of stature is hypernormal. The cause of
this is discussed.

Résumé.

Il est démontré que dans un grand nombre de recherches anthro-
pométriques, la distribution concernant la stature est hypernormale;
la raison en est discutée.

Zusammenfassung.

Es wird gezeigt, daß in einer großen Anzahl von anthropo-
metrischen Untersuchungen die Verteilung der Körperlänge über-
normal ist. Die Ursache hiezu wird diskutiert.